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Prognosis with Many Positive Nodes in Otherwise Favorable-Stage Differentiated Thyroid Cancer

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Purpose

In patients with well-differentiated thyroid cancer, there is controversy about the prognostic importance of a large number of positive neck nodes. The purpose of this study was to evaluate the issue among a group of patients for whom it is of most clinical importance, those with classic histology and favorable T stage. There are no published data on this focused subject. Our hypothesis was that the recurrence rate would be high in patients with many positive nodes.

Method

Our study population included 25 patients who met the following inclusion criteria: Classic-histology papillary or follicular thyroid carcinoma treated with total thyroidectomy and neck dissection followed by adjuvant I-131 treatment in our department between January 1, 2003, and December 31, 2013; adult age of > 18 years; and AJCC stage (8th edition) of T0-3 N1b, with at least 5 positive nodes, and M0.

Results

The median positive node number was 10 (range, 5-31). The median adjuvant I-131 dose was 158 mCi (range, 150-219 mCi). The median follow-up in patients without a recurrence after treatment was 7.3 years. The 10-year actuarial results were good: Overall survival was 100% and freedom from recurrence 72%; freedom from recurrence at last follow-up (following salvage therapy) was 92%. There was no statistically significant association between positive node number, or extranodal extension, and recurrence rate.

Conclusions

These results contradict our hypothesis of a poor prognosis with many positive nodes in patients with favorable T stage well-differentiated thyroid cancer. Recurrence was unusual following moderate-dose adjuvant I-131 treatment and most recurrences were successfully salvaged. These results are valuable in directing initial adjuvant therapy and follow-up intensity. Our results do not inform the question of the use of postoperative thyroglobulin (Tg) level to select N1b patients for low-dose I-131 treatment.

Categories

Clinical investigations

4

Palliative radiotherapy for bony metastases from GI tumors: sociodemographics,
disparities, and the percentage of remaining life spent receiving treatment

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Purpose

To evaluate the use of palliative radiotherapy (pRT) for osseous metastases among patients with gastrointestinal malignancies by sociodemographic factors, tumor type, and survival.

Method

The NCDB was used to identify 9297 patients with GI cancers who received pRT to bony metastases from 2004 to 2013. Cancers included esophageal, stomach, pancreatic, hepatocellular (HCC), bile duct & other, gallbladder, colon/sigmoid, and rectal. 5774 remained after excluding incomplete data. Strata included age, race, sex, household income, Charlson-Deyo score (CDS), site of metastasis, Insurance status, treatment facility type, and distance from treatment site (crow-fly). Outcomes of interest included survival after diagnosis, survival after pRT, completion of pRT, and percent of remaining life spent receiving radiotherapy (PRLSRT). Chi-squared, Kaplan Meier curve with log-rank analyses, and Cox Regression evaluated outcomes as a factor of sociodemographics.

Results

Patients were 69% male, 81% Caucasian (CA) and 13% African American (AA). The most commonly used pRT regimen was 30Gy in 10 fractions, and single-fraction 8Gy was increasingly utilized towards 2013. As survival decreased, use of single-fraction pRT increased indicating appropriate pairing of treatment duration to prognosis. This trend was consistent among both AA and CA patients.

AA patients were younger (58.9 vs 64.1 p<0.001), and more likely to live <20mi from their treatment facility compared to CA’s. AA’s were more likely to have no insurance or Medicaid (9.7% vs 5.3%, or 18.1% vs 8% p<0.05) compared to CA’s. AA’s were less likely to have pancreatic cancer. Slightly more AA’s completed pRT than CA’s (69.2% vs 65.2%, p<0.05), and had longer survival after diagnosis compared to CA (10.2 vs 9.7 months) but shorter survival after pRT suggesting a delay in palliation. Additionally, those who lived 40-60 miles from treatment facility had higher mean survival. Patients with private insurance had better 10mo survival. Patients treated at integrated network programs had early survival advantages.

PRLSRT did not differ by race but decreased from 2004 to 2013 suggesting improvements in palliation with shorter fractionation. PRLSRT>50% (p50) did not differ by crow-fly or facility type, but those with Medicare were more likely to have p50 compared to Medicaid (19.2% vs 13.0%, p<0.001). Men were more likely to have p50 compared to women (17.1% vs 14.7%, p=0.019). A PRLSRT of 10% or less (p10) was more frequent in those who lived 60mi or more from treatment, were treated at an academic facility, had private insurance, or a lower CDS. Axial skeleton metastases had a higher p50. Sites with higher p10 were the extremities, shoulders, and ribs.

Conclusions

This study evaluated trends of pRT use among patients and stratified analyses by sociodemographic factors. Further research may uncover potential methods to optimize the use of pRT.

Categories
Socioeconomic/ethical issues/health outcomes research

Palliative radiation treatment for previously untreated incurable head and neck cancer: A review

Toms Vengalloor Thomas, Teessa Perakattu Kuruvilla, Eldrin Bhanat, Anu Abraham, Sataseelan Packianathan, Srinivasan Vijayakumar

University of Mississippi Medical Center, Jackson, MS, USA

Purpose

Currently, there are no evidence-based guidelines regarding palliative radiation for untreated, incurable head and neck squamous cell carcinoma (HNSCC) patients.

Method

Articles published between 1980 and 2018 were selected from an English Medline literature search using the following keywords: Palliation of incurable head and neck cancer, palliative radiation, Quality of Life (QOL).

Results

A few phase II and several retrospective studies have reported data on palliative radiation dose and fractionation schedules for patients with incurable head and neck cancer. These studies included a heterogeneous patient population and are listed in the table as below.
<table>
<thead>
<tr>
<th>Name</th>
<th>Total dose</th>
<th>Fractionation</th>
<th>RT technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>QUAD SHOT</td>
<td>42 Gy</td>
<td>3.5 Gy BID x 2 days</td>
<td>3-D CRT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Repeated q4 weeks interval x 2 times</td>
<td></td>
</tr>
<tr>
<td>Hypo Trial</td>
<td>30 Gy</td>
<td>6 Gy per fraction x 5 fractions, 2 fractions per week</td>
<td>2-D and 3-D CRT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Optional boost of 6 Gy if &lt;3 cm</td>
<td></td>
</tr>
<tr>
<td>Canadian (Fortin et al)</td>
<td>25 Gy</td>
<td>5 Gy in 5 daily fractions in 1 week</td>
<td>IMRT</td>
</tr>
<tr>
<td>Princess Margaret Hospital (Canada)</td>
<td>50 Gy</td>
<td>2.5 Gy daily x 10 fractions in 2 weeks</td>
<td>2-D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Repeated once after a 2-week break</td>
<td></td>
</tr>
<tr>
<td>AIIMS (India)</td>
<td>20 Gy</td>
<td>4 Gy daily in 5 fractions over 1 week</td>
<td>2-D and 3-D CRT</td>
</tr>
<tr>
<td>Tata Memorial (India)</td>
<td>40 Gy</td>
<td>2.5 Gy daily in 16 fractions</td>
<td>2-D and 3-D CRT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 Gy boost if partial response</td>
<td></td>
</tr>
<tr>
<td>RTOG 85-02</td>
<td>44.4 Gy</td>
<td>3.7 Gy BID x 2 days</td>
<td>2-D Initially</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Repeated q2-3 weeks x 2 times</td>
<td>3-D CRT</td>
</tr>
<tr>
<td>Christie’s Regimen (England)</td>
<td>50 Gy</td>
<td>3.125 Gy daily x 16 fractions</td>
<td>3-D CRT</td>
</tr>
<tr>
<td>UK regimen</td>
<td>40 Gy</td>
<td>4 Gy daily x 5 fractions in 1 week</td>
<td>3-D CRT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Repeat after a 2-week break</td>
<td></td>
</tr>
<tr>
<td>SCAHRT (USA)</td>
<td>60-72 Gy</td>
<td>3 Gy daily x 10-12 fractions</td>
<td>3-D CRT initially</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Repeat after 3-5 weeks</td>
<td>IMRT more recently</td>
</tr>
<tr>
<td>Danish</td>
<td>52-56 Gy</td>
<td>4 Gy per fraction, 2 fractions per week</td>
<td>IMRT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total 13 - 14 fractions</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions**

There are multiple-dose fractionation regimens currently being used for palliative radiation treatment. For patients with an oligometastatic disease with excellent performance status (ECOG 0-1), an aggressive approach with higher doses should be considered, whereas, for patients with poorer performance status (ECOG ≥2), an abbreviated course of radiation treatment may achieve the goals of palliation.

**References**


**Categories**

Socioeconomic/ethical issues/health outcomes research
Aggressive palliation of incurable head and neck cancers with concurrent chemoradiotherapy: A review

Toms Vengaloor Thomas, Teessa Perekattu Kuruvilla, Eldrin Bhanat, Satyaseelan Packianathan, Srinivasan Vijayakumar

University of Mississippi Medical Center, Jackson, MS, USA

Purpose

For previously untreated, incurable head and neck squamous cell carcinoma (HNSCC) patients, the standard of care is palliative chemotherapy. A prior analysis of the National Cancer Data Base (NCDB) suggested that the aggressive treatment of patients with metastatic HNSCC using combined high intensity local treatment (radiation dose >60 Gy or oncologic resection of the tumor) had improved survival in comparison to patients receiving systemic therapy alone. We reviewed the literature more extensively to investigate the role of more aggressive palliation with chemoradiotherapy in these patients.

Method

Articles published between 1980 and 2018 were selected from an English Medline literature search using the following key words/phrases: Palliation of incurable head and neck cancer, palliative chemoradiation.

Results

We identified 4 retrospective studies reporting data on palliative chemoradiotherapy for patients with incurable head and neck cancers, the details of which are outlined in the table below.

<table>
<thead>
<tr>
<th>Study</th>
<th>Author</th>
<th>Patient characteristics</th>
<th>Total dose</th>
<th>Fractionation</th>
<th>Technique</th>
<th>Concurrent chemo</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHF2SQ</td>
<td>Monnier et al.</td>
<td>72 patients; 90% with KPS &gt;70%</td>
<td>48 Gy</td>
<td>3 Gy BID on 1st and 3rd day; Repeated q2 weeks x 4.</td>
<td>3-D CRT</td>
<td>Yes Platinum based</td>
</tr>
<tr>
<td>Italian</td>
<td>Minatel et al.</td>
<td>62 patients; Median KPS 60 (50-90%)</td>
<td>50 Gy</td>
<td>Split course 2.5 Gy daily, over 2 weeks; Repeated after 2 weeks.</td>
<td>2-D RT</td>
<td>Yes Bleomycin (10 mg)</td>
</tr>
<tr>
<td>Modified</td>
<td>Gamez et al.</td>
<td>21 patients; ECOG 0-3</td>
<td>44.4 Gy</td>
<td>3.7 Gy BID x 2 days; Repeated q4 weeks x 3.</td>
<td>3-D CRT or IMRT</td>
<td>Yes Carboplatin (AUC 2)</td>
</tr>
<tr>
<td>Indian</td>
<td>Dubey et al.</td>
<td>60 patients; All with KPS &gt;70%</td>
<td>44.4 Gy</td>
<td>3.7 Gy BID x 2 days; Repeated q3 weeks x 3.</td>
<td>2-D RT</td>
<td>Yes Paclitaxel 60 mg/m²</td>
</tr>
</tbody>
</table>

Conclusions

Although limited, there is published evidence to suggest that palliative chemoradiotherapy may improve survival for patients with incurable head and neck cancers. This approach can be considered as a treatment option for patients with good performance status and limited metastatic disease.

References

1. Monnier L, Touboul E, Durdux C, Lang P, St Guily JL, Huguet F.


**Categories**

Clinical investigations

**7**

**Stereotactic Body Radiation Treatment (SBRT) for palliation of previously untreated, incurable head and neck cancer: Is there evidence for this approach?**

Toms Vengaloor Thomas, Teessa Perekattu Kuruvilla, Eldrin Bhanat, Satyaseelan Packianathan, Srinivasan Vijayakumar

University of Mississippi Medical Center, Jackson, MS, USA

**Purpose**

Stereotactic Body Radiation Treatment (SBRT) has established itself as a re-irradiation modality for previously treated head and neck cancer. There are only limited data, however, for its use as the primary treatment for palliation of previously untreated, incurable head and neck cancers.

**Method**

Articles published between 2000 and 2018 were selected from an English Medline literature search using the following keywords: Palliation of incurable head and neck cancer, Stereotactic Radiation, SBRT for palliation.

**Results**

There are a few small, retrospective studies published where SBRT was used as the modality of treatment for palliation of head and neck cancer. Patients were elderly with small tumors or others who refused standard treatment. Most of them had a small volume of disease. The studies and the radiation fractionation schedules are listed in the table below.
### Conclusions

SBRT appears to be a feasible treatment option for selected patients with a small volume of disease who are ineligible for curative treatment or who refuse standard therapy.

### References


### Categories

Clinical investigations

### Impact of Antibiotic Usage on Treatment Response During Checkpoint Inhibitor Treatment of Non-Small Cell Lung Cancer

**Cory Hogue**, Timothy Kuzel, Jeffrey Borgia, Gaurav Marwaha, Philip Bonomi, Mary Jo Fidler, Marta Batus, Dian Wang, Parul Barry

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**Purpose**

Growing evidence suggests that the gut microbiome may influence response to checkpoint inhibitor (CPI) therapy. Antibiotics alter the gut microbiome and their use prior and during therapy may be prognostic.

**Method**

This is an IRB approved retrospective study. Patients with non-small cell lung cancer treated with CPI were identified from an institutional database. Demographics, antibiotic usage, radiation utilization, and cancer-related outcomes were recorded and analyzed. Cox proportional hazard models adjusted for age at diagnosis and sex were performed.

**Results**

161 patients met inclusion criteria for this analysis and were treated with CPIs from 2015 to 2019. Median age was 66 years old (range 46-88) and 60% were female. Most patients had prior separate lines of systemic therapy.
therapy (median 2 lines, range 1-4). Histological subtypes included adenocarcinoma (70%), squamous cell carcinoma (24%) and other histologies (6%). Median CPI treatment length was 2 months. CPIs included Nivolumab and Pembrolizumab. 58 patients (36%) had antibiotic usage in the 90 days prior to checkpoint inhibitor initiation. 33 patients (20%) used antibiotics during CPI treatment. 71 patients (44%) had no antibiotic usage prior or during CPI treatment. 110 patients (68%) received radiation treatment prior, during or after completing CPI therapy. There were no progression free survival differences for patients receiving antibiotics in the 90 days prior to treatment start (HR 1.024, p=0.92). The use of antibiotics during therapy was associated with increased progression free survival (HR 0.597, p=0.02). There were no overall survival differences for patients receiving antibiotics in the 90 days prior to CPI therapy (HR 1.122, p=0.64). The effect of antibiotic utilization on overall survival was not significant (HR 0.660, p=0.07).

Conclusions
Antibiotic use during CPI therapy was not associated with decreased progression free and overall survival in our heavily pre-treated patient population. Improved progression free survival and a trend toward improved overall survival were noted. Further studies are needed to determine the relationship between duration of CPI treatment and antibiotic utilization.

Categories
Clinical investigations

Single fraction stereotactic radiosurgery vs fractionated radiotherapy for the treatment of metastatic brain tumors: a comparative analysis of local control and risk of radiation necrosis

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2Renown Cancer Institute, Reno, Nevada, USA

Purpose
Brain metastases are a common debilitating neurological complication of cancer affecting 15-30% of patients. Current treatment includes resection, systemic therapy, whole brain radiation therapy (WBRT), stereotactic radiosurgery (SRS), and fractionated stereotactic radiotherapy (FSRT). The main limiting factor in SRS and FSRT treatment is radiation necrosis (RN). Radiation necrosis reports range from 1.5% to over 30%. Identifying contributing factors continues to be an area of need for investigation to improve patient care and decrease additional procedures and treatment.

Method
We performed a retrospective chart review of patients receiving SRS or FSRT for the treatment of metastatic brain tumors from 2016-2019. Only patients with at least 3-months follow-up time were included in the study. Surgical pathology, clinical presentation, and/or MR-Imaging was used to identify patients with a diagnosis of radiation necrosis. Factors influencing radiation necrosis free survival were analyzed using cox proportional hazards model. The impact of treatment type on tumor progression was assessed using a student’s t-test.

Results
Of the 53 participants included in our study, 33 presented with multiple metastases, amounting to a total of 101 tumors treated with SRS (n=62) or FSRT (n=39). The average follow-up time of participants was 10-months. The average PTV for tumors treated with SRS was 1.59 cc (range 0.03 - 9.9 cc), versus 19.15 cc (range 1.0 - 151 cc) for those treated with FSRT. Tumors treated with FSRT showed a rate of local control (87.2%) equivalent to those treated with SRS (87.1%) (p = 0.616). Of the 101 tumors receiving treatment, 17 (16.8%) developed radiation necrosis. The incidence of radiation necrosis was higher in the SRS group (17.7%) than the FSRT group (15.4%). Multivariate cox proportional hazards analysis revealed number of fractions (HR 0.16, 95% CI 0.03 – 0.92, p = 0.040) and tumor PTV (HR 1.07, 95% CI 1.02 – 1.11, p = 0.003) as predictors of radiation necrosis free survival. Metastasis number, age, total radiation dose, prior WBRT, surgical treatment, sex, and maximum radiation dose were not identified as significant.

Conclusions
Radiation necrosis is the major side effect of SRS and FSRT treatment requiring more information and research into differing prognostic factors leading to the development of RN. We found that fractionation and PTV were the most statistically significant factors influencing the development of RN using a Linac based treatment. Using FSRT over SRS for the treatment of brain metastasis allows safer treatment to much larger areas,
without sacrificing local control, and decreasing the rates of radionecrosis.

**References**


**Categories**

Clinical investigations

13

**Unforeseen Computed Tomography Re-simulation for Initial Radiation Planning: Associated Factors and Clinical Impact**

April Metzger

Allegheny Health Network, Pittsburgh, PA, USA

**Purpose**

Repeat CT simulation is problematic due to additional expense of clinic resources, patient inconvenience and treatment delay. We investigated the factors and clinical impact of unplanned CT re-simulations in our network.

**Method**

We utilized the billing records of 18,170 patients treated at 5 clinics. Two hundred thirteen patients were re-simulated prior to their first treatment. The disease site, location, use of four-dimensional CT (4DCT), use of contrast, image fusion, and cause for re-sim were recorded. Odds ratios (OR) were used to determine statistical significance.

**Results**

Our total rate of re-simulation was 1.2%. “Anal/colorectal” (OR = 2.72, 1.73 – 4.30) and “head & neck” (OR = 2.67, 1.70 – 4.22) disease sites had higher rates of re-simulation. “Brain” (OR = 0.38, 0.22-0.66) and “lung/thorax” (OR = 0.48, 0.28-0.82) had lower rates of re-simulation. The most common causes for re-simulation were: set-up change (11.7%), change in patient anatomy between simulation and treatment (9.8%), and rectal filling (8.5%). The re-sim rate for 4DCTs was 3.03% compared to 1.0% for non-4DCTs (P < 0.001). No difference was seen between academic and community settings. Median time between initial simulation and re-sim was 7 days.

**Conclusions**

At our institution, the most common sites for re-simulation were anal/colorectal and H&N, largely because of setup error or changes in anatomy. 4DCT technique during initial simulation correlated with higher re-simulation rates. The re-simulation rate was low at 1.2%, and resulted in a median treatment delay of 7 days. Further QA studies are warranted to limit re-simulation, treatment delays, patient inconvenience, and additional costs.

**Categories**

Socioeconomic/ethical issues/health outcomes research

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**Atlas Based Segmentation in Prone Breast Cancer Radiation Therapy**

William Stross, Steven Herchko, Laura Vallow

Mayo Clinic, Jacksonville, FL, USA

**Purpose**

Contouring is the single most time consuming non-patient facing task a radiation oncologist performs (1). We sought to optimize radiation oncology treatment planning workflow efficiency. Specifically, we aimed to decrease physician time spent contouring organs at risk (OAR) and clinical target volume (CTV) targets within the early stage breast cancer patient population while not sacrificing on the quality of radiation volumes utilizing atlas based segmentation (ABS) software. Prior studies across different cancer sites report 26-63% reduction in physician contouring time with this type of advanced software (2-4).

**Method**

An atlas of 20 previously treated patients with early stage breast cancer was generated using MIM Maestro ABS software. Then a sample of 20 separate patients was evaluated using our standard departmental workflow with and without incorporation of the ABS software. The manual contouring time and initial target volumes served as the baseline measurements. These were then compared to the edited and unedited ABS generated volumes. Dice coefficient (DC), logit transformation of DC (logit(DC)), and mean distance to
agreement (MDA) were used to objectively compare volumes. Subjective quality of the contours was analyzed with an independent physician review.

Results

The contouring physician edited 89% of OAR volumes on average per patient, whereas the independent reviewing physician recommended revision of 28% OAR on average volumes per patient. CTV editing was performed in 20/20 (100%) of cases by the contouring physician, whereas CTV revision was recommended by the independent reviewing physician in 4/20 (20%) of cases. Our atlas performed well with DC values of >0.909 and logit(DC) of >2.344 across heart, lung, and breast volumes when compared to manually generated volumes. All objective measurements demonstrated improvement with physician refinement of ABS generated volumes. The largest absolute improvement was seen in the heart and breast CTV targets. There was 100% acceptance of the edited ABS generated volumes by the independent reviewing physician. The average time saved using ABS was 6.27 minutes (57%) per patient.

Conclusions

This study confirms ABS offers improvements in efficiency without sacrificing contour quality in the early stage breast cancer patient population and demonstrates the functionality of ABS with prone patient positioning.

References

1. Blank (2012) "Evaluation of time, attendance of medical staff, and resources during radiotherapy for breast cancer patients" Strahlentherapie und Onkologie 188


Categories

Physics/technology

15

The Role of Adjuvant Radiation in Lymph Node Positive Pancreatic Cancer Patients

Fan Zhu, Haoyu Wang, Adel Guirguis, Hani Ashamalla

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Purpose

To determine the impact of adjuvant radiation therapy (RT) on overall survival (OS) in different lymph node status groups (represented by number of positive lymph nodes (NPN) and lymph node ratio (LNR)) in pancreatic cancer (PCa) patients who received adjuvant chemotherapy. LNR is defined as NPN divided by number of total lymph nodes examined (TNE).

Method

National Cancer Database was queried for non-metastatic, pathology-proven invasive PCa patients from 2004 to 2015. Exclusion criteria include inadequate resection, more than 12 weeks delay between surgery and chemotherapy and receipt of hormonal or immunotherapy. Data were analyzed according to demographic characteristics, tumor characteristics, treatment modalities and survival statistics. Cox models were utilized to assess the effect of RT after accounting for multiple confounders. Interaction terms were applied to evaluate the effect of RT in different NPN, LNR, and margin status strata. Propensity score matching was not used because the data from national database was representative, and the sample of the patients who received RT and that of patients who did not were balanced. Multivariate analysis was performed to adjust for the effect of covariates and no additional samples needed to be dropped.

Results

Of 19759 patients identified, 11908 patients met all criteria. 998 patients were further excluded due to unknown staging, margin status or grade information. For LNR analysis, 35 patients with missing TNE data were excluded (N=10875).

For patients with negative margins, adjuvant radiation did not improve OS when NPN was 0 (HR=1, p = 0.95) nor did it significantly improve OS when NPN was 1 (HR=0.93, p=0.38); adjuvant RT improved OS when NPN was 2-3 (HR=0.84, p=0.01) or LNR was 0.15-0.25 (HR: 0.79,
p=0.002); adjuvant RT marginally improved OS when NPN was ≥4 (HR: 0.88, p=0.08) or LNR was 0.25-1 (HR: 0.89, p=0.096).

For patients with positive margins, adjuvant RT improved OS but it was not significant when NPN was 1-3 (HR=0.89, p=0.36) or when NPN was ≥4 (HR=0.79, p=0.07); likewise, adjuvant RT did not significantly improve survival when LNR was 0.15-0.25 (HR: 0.85, p=0.28) or 0.25-1 (HR: 0.79, p=0.07).

Conclusions
In PCa patients with negative surgical margins who received adjuvant chemotherapy, adjuvant RT had the most survival benefit with 2-3 positive lymph nodes or LNR of 0.15-0.25. In patients with positive surgical margins, adjuvant RT numerically improved survival when there were positive lymph nodes.

Categories
Clinical investigations
17

Incidence and course of Grade 2 proctitis with the use of modern IMRT and brachytherapy for localized prostate cancer in a community cancer center

Amy Rao1, Mary Rachel Bonner2, Nolf Tanner1, Myers Stephanie3, Morris Chris3, Tom Bozzuto4, Michael Monahan1, Charles Mendenhall1, William McAfee5, Daniel A. Jones4

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Purpose
The purpose of this study was to retrospectively review and characterize the course of treatment for patients who developed Grade 2 radiation proctitis who were treated definitively for prostate cancer. In this study, we also attempted to correlate patient and treatment risk factors with an increased likelihood of developing Grade 2 toxicity.

Method
Charts of all 237 consecutive prostate cancer patients treated with IMRT and/or brachytherapy seed implant from March 2014 to March 2017 at a community hospital were retrospectively reviewed. Median follow up was 18 months.

Patient factors assessed included use of anticoagulants or antiplatelet therapy, race (African American vs. non), presence of diabetes, overall risk stratification of cancer. Treatment factors assessed included use of androgen deprivation therapy (ADT), technique (implant alone vs. IMRT vs. IMRT/Implant), and Field size (pelvic field vs. local field only). G2 proctitis as a function of selected prognostic factors was assessed with Fisher’s Exact Test. CTCAE V 4.0 grading scale was used to classify proctitis, with further classification of category 2 (2A medicinal, 2B argon plasma coagulation (APC)/local intervention, and 2C (hyperbaric oxygen (HBO).)

Results
Overall rate of G2 proctitis was 6.3%. This was further classified as 2A (2.1%) 2B (2.5%) and 2C (1.7%). Management of symptoms was initiated on average at 14 months from completing treatment. Proctitis resolved completely or was downgraded in all patients. On average, proctitis resolved at 12 months with medicinal use, 6 months after APC, and 4.5 months after HBO.

Patient factors did not increase the risk of G2 proctitis by univariate analysis. These include chronic use anticoagulants or antiplatelet therapy (p=0.43), Race (p=0.98), presence of diabetes (p=0.45), and overall risk group (0.09). Treatment factors also did not increase the risk of G2 proctitis by univariate analysis. These include use of ADT (p=0.13), Technique (p=0.12) and Field size (p=0.63).

Conclusions
With the use of modern treatment techniques, Grade 2 proctitis was seen in 15 (6.3%) patients, all of which experienced resolution or downgraded symptoms within 4-12 months of intervention. While there were no statistically significant risk factors for developing proctitis, certain factors trended and provide directions for future research in defining a high risk population, such as technique, overall risk group, and use of ADT.

Categories
Translational science
18

Comparison of Radical Prostatectomy versus Radiation and Androgen Deprivation Therapy Strategies as Primary Treatment for High-Risk
Localized Prostate Cancer: a Systematic Review and Meta-analysis

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Purpose

There is little level 1 evidence regarding the relative efficacy of radical prostatectomy (RP) compared to radiotherapy (RT) combined with androgen deprivation therapy (ADT) for high-risk prostate cancer. As such we have conducted a systematic review and meta-analysis comparing overall and prostate cancer-specific mortality (OM and PCM) among patients with high-risk prostate cancer treated with RP or RT/ADT, including consideration of combined modality therapies including RT with brachytherapy boost.

Method

We searched Pubmed, Scopus, and the Cochrane Library through July 2019 covering a period since 2009. We report the results of our systematic search according to recommendations from the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement. Hazard ratios (aHRs) were extracted for each endpoint. The risk of bias was assessed using the Newcastle-Ottawa Scale.

Results

23 studies with low to moderate risk of bias were found meeting inclusion criteria. In keeping with prior studies external beam radiotherapy (XRT) without specification of ADT was associated with worse OM and PCM (aHR 1.65, 95% CI 1.42-1.91, p < 0.0001; I² = 53.4%) and (aHR 1.90, 95% CI 1.61-2.23, p < 0.0001; I² = 50.4%). These associations were weaker though not entirely eliminated when comparing XRT/ADT vs. RP (PCM aHR 1.54, 95% CI 1.16-2.04, p = 0.002: I² = 61.5%). Combination XRT with brachytherapy (MaxRT), on the other hand, was associated with improved PCM compared to RP (aHR 0.48, 95% CI 0.30-0.78, p = 0.003: I² = 23.8%), an effect that was not significant when comparing MaxRT to combination RP/adjuvant RT (aHR 0.81, 95% CI 0.59-1.11, p = 0.197: I² = 0%).

Conclusions

Evidence demonstrating definitive superiority of either modality is lacking. Recent studies demonstrate improved consideration of ADT, radiation dose, brachytherapy boost, and utilization of postoperative adjuvant radiation. Residual confounding continues to limit the interpretation of observational data.

Categories

Clinical investigations

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The impact of prior prostatectomy on the detection of prostate cancer recurrence with ¹⁸F-fluciclovine: Imaging results from the FALCON trial

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Purpose

An estimated 40–60% of patients will develop biochemical recurrence (BCR) of prostate cancer after radical prostatectomy (RP). Early and accurate localisation of lesions in such patients will help guide salvage therapy decisions. Conventional imaging has limited utility for the detection of sites of recurrence, especially when prostate-specific antigen (PSA) levels are low. ¹⁸F-Fluciclovine is a positron emission tomography (PET) tracer that has been demonstrated to detect recurrence across a wide-range of PSA values. It is approved for use in Europe and the USA for localisation of metastases in patients with suspected prostate cancer recurrence. FALCON (NCT02578940) was a UK-based, multicentre prospective trial that assessed the impact of ¹⁸F-fluciclovine PET/CT on the management of men with BCR after curative-intent treatment of prostate cancer. The present analysis evaluates imaging findings from FALCON to report ¹⁸F-fluciclovine detection rates (DRs) among patients with and without prior RP.

Method

Eligible men (≥ 18 years; ECOG 0-2; first episode of BCR following radical curative-intent therapy; being considered for salvage treatment; no androgen-deprivation therapy in the 3 months before screening) underwent ¹⁸F-fluciclovine PET/CT according to standardised procedures at one of 6 UK sites. Imaging results were stratified by the patients’ prior therapy and baseline characteristics.

Results

In total, 104 evaluable patients (median PSA, 0.79 ng/mL) underwent ¹⁸F-fluciclovine PET/CT between December 2015 and May 2017. The patients were a median 58 months...
post-initial diagnosis and 65 (63%) previously had RP. Median PSA levels were higher among the intact prostate group (see table).

Overall detection was broadly proportional to PSA. $^{18}$F-Fluciclovine detected lesions in 58/104 (56%) patients. The DR was lower in those who had undergone RP (21/65; 32%) compared with that in the intact prostate group (37/39; 95%).

<table>
<thead>
<tr>
<th></th>
<th>Prior RP</th>
<th>Intact prostate</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>65</td>
<td>39</td>
<td>104</td>
</tr>
<tr>
<td>PSA, ng/mL:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>0.63±0.91</td>
<td>7.15±6.07</td>
<td>3.08±4.92</td>
</tr>
<tr>
<td>Median (range)</td>
<td>0.32 (0.04–6.10)</td>
<td>4.90 (1.74–28.00)</td>
<td>0.79 (0.04–28.00)</td>
</tr>
<tr>
<td>Gleason score, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤6</td>
<td>4 (6.2)</td>
<td>12 (31)</td>
<td>16 (15)</td>
</tr>
<tr>
<td>7</td>
<td>49 (75)</td>
<td>23 (60)</td>
<td>72 (69)</td>
</tr>
<tr>
<td>≥8</td>
<td>1 (1.5)</td>
<td>2 (5.1)</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Missing</td>
<td>11 (17)</td>
<td>2 (5.1)</td>
<td>13 (13)</td>
</tr>
<tr>
<td>Overall detection rate, n (%)</td>
<td>21 (32)</td>
<td>37 (95)</td>
<td>58 (56)</td>
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<tr>
<td>Detection rate by PSA in ng/mL, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–0.5</td>
<td>13/45 (29)</td>
<td>0/0 (0)</td>
<td>13/45 (29)</td>
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<tr>
<td>&gt;0.5–1.0</td>
<td>4/11 (36)</td>
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<td>0/1 (0)</td>
<td>1/5 (20)</td>
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<tr>
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<td>3/4 (75)</td>
<td>19/20 (95)</td>
<td>22/24 (92)</td>
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<tr>
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<td>0/1 (0)</td>
<td>10/10 (100)</td>
<td>10/11 (91)</td>
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<tr>
<td>&gt;10.0</td>
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<td>8/8 (100)</td>
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</tr>
</tbody>
</table>

Conclusions

$^{18}$F-Fluciclovine PET/CT detected lesions in the majority of men with their first episode of BCR following curative-intent primary therapy. The DR increased with increasing PSA and was higher among patients with intact prostate than those who had previously undergone RP.

Categories

Clinical investigations

Locally Advanced Gynecologic Malignancies: Six Year Update of Initial Experience


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**Purpose**

Delivery of high dose radiation within a prescribed period of time is associated with local control when treating primary or recurrent gynecologic cancers. Not all patients are eligible for a brachytherapy boost. We update our experience using stereotactic body radiotherapy (SBRT) boost as an alternative.

**Method**

From 2012 to 2014 eight patients with locally advanced squamous cell carcinoma of the uterine cervix, recurrent endometrial cancer at the vaginal cuff, or primary vaginal cancer received an SBRT boost after pelvic external beam (EBRT) radiotherapy (45-50 Gy). One patient received SBRT after EBRT and 2 HDR brachytherapy fractions. Patients either refused brachytherapy or were unsuitable from medical comorbidities. Patients were immobilized using a CIVCO body frame (CIVCO medical solutions, Coralville, IA) with abdominal compression. Vaginal and fiducial markers were used to localize tumor at simulation and treatment. Doses were prescribed to D90 of the PTV (5 mm expansion on CTV excluding rectum when not involved by tumor). Dose was limited by organ-at-risk tolerances (EQD2Gy D2cc planning objectives included bladder < 90 Gy, rectum < 75 Gy, sigmoid < 75 Gy, small bowel < 60 Gy). The Eclipse planning system was used to generate RapidArc plans with 6 MV photons. Treatment was delivered using a Varian True Beam STx linac. Daily cone beam CTs (CBCTs) were performed using rectum, bladder, visible tumor, and markers for image guidance and ExacTrac (BrainLab, Germany) was used to ensure precision of delivery. Tumor status and toxicities were recorded at regular follow up intervals; toxicity was graded according to CTCAE v. 4.0.

**Results**

Dose/fractionation schemes were 7 Gy x 2 for one patient (after two HDR brachytherapy fractions), 6 Gy x 5 for six pts, and 5.8 Gy x 5 for one pt. Cumulative EQD2Gy to D90 of the target volume ranged from 74.6 Gy to 84.3 Gy (mean 81.3 Gy). Mean D2cc rectum and bladder doses were 66.3 Gy (range 59.4 – 75.8 Gy) and 77.3 Gy (range 69.6 – 83.6 Gy) respectively. Mean overlap between rectum as contoured on daily conebeam CTs and the PTV was 0.29 cc (range 0.00 – 1.42 cc). Two local recurrences were noted at a median follow up of 74.6 months. The patients recurred at 16 months and the other at 34 months. One of these patients went on to develop distant metastatic disease and one was salvaged with surgery and has no evidence of disease. One patient developed distant metastases at seven months. One patient developed a rectovaginal fistula requiring surgical intervention after developing distant metastatic disease at 2 years. Two patients developed grade 3 vaginal stricture (inability to visualize vaginal apex/cuff on exam).

**Conclusions**

SBRT should not be used as a substitute for brachytherapy boost unless there are absolute contraindications to interstitial brachytherapy delivery.

**Categories**

Clinical investigations 22

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**Prescribing Patterns of Radiation Oncologists for Medicare Patients**

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**Purpose**

Concerns about high and rapidly rising drug costs have increased scrutiny on physician prescribing patterns of prescription medications. The release by the Centers for Medicare and Medicaid Services (CMS) of the Medicare Part D Prescriber Public Use Files (MPDPUF) allows the public to view prescribing patterns of individual physicians to patients in the Medicare Part D system. The purpose of this analysis is to describe prescribing patterns of radiation oncologists nationally.

**Method**

The MPDPUF 2017 was queried for prescribing patterns by radiation oncologists in 2017. We report the total cost of all medications prescribed by radiation oncologists as well as the distribution of cost among physician prescribers.

We reported the ten most commonly prescribed medications and the ten most expensive medications (by total cost to the Medicare Part D system). The total cost is reported as the aggregate drug cost paid for all associated claims by the Part D plan, Medicare beneficiary, government subsidies, and any other third party payers.

**Results**

In 2017, the total cost of medications prescribed by radiation oncologists for
patients using Medicare Part D was $21,268,688. 9.8 million total days of supply were prescribed. There were 4,604 unique physician NPI numbers identified for radiation oncology. Twelve physicians (0.26%) prescribed $10,900,634 (51%) worth of medications. 294 physicians (6.4%) prescribed 4.9 million (50%) total days of supply.

In 2017, the most commonly prescribed medications, in order of total days of supply include tamsulosin (4.69 million), biclutamide (0.47 million), levothyroxine (0.32 million), hydrocodone-acetaminophen (0.29 million), dexamethasone (0.28 million), oxycodone (0.16 million), finasteride (0.16 million), anastrazole (0.15 million), gabapentin (0.14 million), and lidocaine HCl viscous (0.12 million). By cost, the most expensive medications include Xtandi ($3.00 million), Subsys ($2.74 million), Zytiga ($2.60 million), tamsulosin ($2.31 million), Zostavax ($2.74 million), Zytiga ($2.60 million), acetylcysteine ($2.31 million), and oxycodone ($2.20 million).

**Categories**

Socioeconomic/ethical issues/health outcomes research

**Conclusions**

This analysis displays the scope of practice with regards to the prescribing patterns of radiation oncologists nationally as well as the large differences in practice patterns. Medication costs are largely driven by a few radiation oncologists, with 0.26% of practicing radiation oncologists driving over 50% of the total cost to Medicare Part D. Tamsulosin is the most commonly prescribed medication by radiation oncologists, with nearly 10x pills dispensed compared to the second most common medication. Several of the most high cost medications include brand name medications for prostate cancer, such as Xtandi and Zytiga, as well as brand name opioid pain medications (Subsys fentanyl sublingual spray).

**Three Dimensional (3D) Printer-Assisted Pelvic Phantom Simulator: Enhancing Resident Training in Prostate Brachytherapy**

**David Byun, David Barbee, Andrew Evans, Kevin Du**
NYU Langone Health, New York, NY, USA

**Purpose**

Prostate brachytherapy is a well-established treatment modality for the treatment of localized prostate cancer patients, either as monotherapy for favorable risk cases or as a boost modality for unfavorable intermediate to high-risk groups. Adequate training is progressively being isolated to a select number of high volume centers, highlighting the need for the development of novel training experiences. To address this, we propose a proof-of-concept study in assessing the feasibility of rapid and cost-effective manufacturing of patient-specific prostate phantoms using commercially available three dimensional (3D) printing techniques and materials for resident brachytherapy education.

**Method**

**Pelvic Phantom Model Production**

Biomaterial similarities between polyvinyl alcohol (PVA) hydrogel and prostate gland as well as silicone rubber for mimicking rectum and bladder have previously been established by Li et al. Pre-implant prostate MRIs of patients previously treated with LDR brachytherapy at our institution will be utilized for segmenting and 3D reconstruction of pelvic organs of interest for phantom model mold creation using available 3D printer computer-aided drafting software.

**Planning, Implantation, and Postimplantation Dosimetry**

Mock treatment planning process with contouring of organs of interest will take place using BK3000 ultrasound system with a transrectal probe by a trainee. The plan will be reviewed using MIM Symphony brachytherapy planning software and ultimately revised and approved by the trainee. Needles and dummy seeds will then be applied using a MICK applicator by the trainee with no direct supervision from senior staff members. The postimplant dosimetric evaluation will be performed using computed tomography simulation scan followed by evaluation of trainee’s pre- and postimplant dosimetric parameters.

**Results**

Results pending - funded by 2019-2020 ACRO Luther Brady Educational Grant

**Conclusions**

With the optimization of the phantom model manufacturing process, completion of proof-of-concept study and future funding opportunities, we hope to expand our phantom simulation project to include our current and future trainees with a long term goal of providing affordable
brachytherapy training system available for multi-institutional collaboration.

References


Categories

Physics/technology

25

Fitting alternative models to linear-quadratic for clonogenic cell survival assays: practical implications of Pool-Repair Lambert and Integrated Michaelis-Menten

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Purpose

Many mathematical models for clonogenic cell survival assays fit experimental data adequately. However, the most commonly used model, the linear-quadratic (LQ) is presumed to diverge at higher values of dose. Two unique three-parameter models, Pool-Repair Lambert (PRL) and Integrated Michaelis-Menten (IMM) has recently been described. The first uses the transcendental function Lambert W, and the second adds a denominator to the traditional LQ model. Both of these models predict cell mortality as log-linear with dose at higher dose levels. The purpose of this investigation is to explore the goodness of fit of these three-parameter models and compare performance to the LQ.

Method

The previously described PRL and IMM models are re-presented here with their mathematical derivation. A large dataset (PIDE) of clonogenic cell survival assays for both photon and particle radiation is used to calculate the parameters of the three compared models. Quantitative statistical analysis is used to describe difference between observed and predicted cell survival across the dose distribution. The difference between the estimates yielded by the two models is described. The relationship between the parameters of each model and the radiation characteristics (e.g. LET) are explored.

Results

The three models all fit the data well. The residual sum of squares is lower for the three-parameter models than it is for the two-parameter LQ model, as would be expected. There does not appear to a striking systematic bias of over-prediction of cell killing by the LQ model even at doses as high as 8-10 Gy.

Conclusions

The difference between the two models is modest at low doses underscored by the fact that the LQ model is actually the second-order Maclaurin series approximation of the PRL model. By the very nature of Maclaurin series, the LQ model is only a good approximation near zero. However, it appears to be a close approximation for the dose levels used in these many studies. While it may be suggested that the LQ model will break down at higher doses (12-20Gy), high dose data was not available for model fitting in this study.

Categories

Translational science

28

Palliative Split-Course pelvic radiotherapy for symptomatic cervical cancer

Eteri Natelauri

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Purpose

Palliative pelvic radiotherapy for cervical cancer is effective in relieving serious pelvic symptoms from tumor bleeding, pain, discharge or mass effect on rectum, genitourinary tract, vessels, and nerves. There’s an absence of an agreement for an optimal palliative RT regimen. We report the outcomes of a split-course
palliative pelvic RT, which is frequently used schema at our institution.

**Method**

Records of 9 patients treated between 2015 and 2019 were reviewed and retrospectively analyzed. Treatment was prescribed to an initial 20 Gy in 5 fractions. After a 2-week rest period, patients were selected to receive an additional 20 Gy. Symptom relief and toxicity throughout RT and once the completion of RT was assessed from physicians’ notes.

**Results**

Durable and timely symptomatic relief was observed in most of the patients. There were no grade 3 to 5 toxicities. Grades 1 GI and GU acute toxicity were observed in 4 patients. G2 acute toxicity was observed in two patients. Three patients did not have any acute side effects. All these patients showed complete symptom remission after treatment.

**Conclusions**

A majority of patients experienced symptomatic improvement. The built-in 2-week break allowed for the selection of patients for high-dose palliative radiation and balanced treatment benefits with potential side effects. This regimen is a viable option for patients who cannot tolerate definitive treatment.

**References**


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**Designing New Rotational Planning Target Volume to Spare Pharyngeal Constrictor Muscles in Patients with Oropharyngeal Cancer**

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1Indiana University, Indianapolis, IN, USA. 2Stony Brook University, Stony Brook, NY, USA

**Purpose**

Intensity-Modulated Radiation Therapy (IMRT) offers dose distributions conformal to the tumor with superior sparing of the organs at risk in head and neck patients. In order not to miss the target, safety margins are applied which account for geometric uncertainties including anatomic motion, delineation errors and setup errors. Currently, uniform margin expansions are used to design standard Planning Target Volume (PTV). Both translations and rotations should be considering in designing PTVs. However, rotations are usually neglected. Reducing the size of isotropic expansion when designing PTVs have been evaluated and a 2mm reduction in the PTV margin can cause less acute dysphagia defined as feeding tube dependence and late dysphagia. The goal of this project is to design a new rotational PTV to spare Pharyngeal Constrictor Muscles (PCMs) with the ultimate goal of reducing acute toxicities including dysphagia.

**Method**

In the first phase of this project, we retrospectively evaluated treatment plans of patients with oropharyngeal cancer and used the cervical spinal longitudinal axis as the axis of rotation to design a new rotational PTV and compare the findings with the standard 3 cm isotropic expansion of the Clinical Target Volume (CTV). We calculated the overlap between the new rotational PTV and PCMs. The next goal is to determine the exact axis of rotation in patients undergoing IMRT. In order to do this, weekly cone beam CT scans of these patients will be evaluated using mathematical techniques, such as Reuleaux theory. The ultimate goal is to design a technique for PTV generation considering patients’ rotation during treatment to enhance radiation dose to the tumor and minimizing the radiation dose to the organs at risk.

**Results**
We retrospectively evaluated 20 patients with oropharyngeal cancer. The new rotational PTV resulted in an average change for overlap between PTV and the superior, middle and inferior constrictor, -37%, -59.4% and -45.2%, respectively. This reduction was more pronounced for patients with base of tongue (BOT) lesion compared to tonsillar lesion. The new rotational PTV caused statistically significant reduction in the superior PCM overlap in the BOT lesions compared to tonsillar lesion, 57.8% versus 25.8%, p=0.01, as well as middle PCM overlap, 73% versus 49%, p=0.04.

Conclusions

This new rotational PTV causes significant reduction of the overlap volume between PCMs and PTVs. The next phase of the project is to look at axis of rotation and dosimetric values.

Categories

Clinical investigations

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Proton Partial Breast Irradiation in a Challenging Location

Danielle Cunningham, Dean Shumway
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Purpose

Early stage breast cancers of the left lower inner quadrant present unique challenges for radiation treatment planning due to proximity to the heart, left anterior descending artery, and contralateral breast.

Method

We present a case of early stage breast cancer of the left lower inner quadrant treated with proton partial breast irradiation.

Results

A healthy 63 year old woman was diagnosed with invasive ductal carcinoma of the left lower inner quadrant identified by routine screening mammography, grade 1, hormone receptor positive, HER2 negative, with Ki-67 of 10%. Lumpectomy demonstrated a 1.7cm tumor with negative margins and a single negative sentinel node. The Oncotype DX recurrence score returned at 10. She was initially recommended whole breast radiotherapy but sought a second opinion due to concern for cardiac exposure to radiation. We considered her a “suitable” candidate for accelerated partial breast radiation according to ASTRO consensus guidelines. At the time of her CT simulation, her tumor was found to be located immediately adjacent to the heart and left anterior descending coronary artery.

She was treated with 2190 cGy in three daily fractions of proton partial breast irradiation with pencil beam scanning proton therapy to the lumpectomy cavity with a 1cm margin. At the time of first treatment, she was noted to have suboptimal alignment of the 3D skin surface in the region of the lumpectomy cavity, likely related to diminishing edema. Pre-treatment verification CT confirmed the need for re-optimization of the proton plan to ensure minimal heart dose. The target volume occupied 24% of her left breast volume, with 99% coverage with 95% of the prescription dose. Her mean heart dose was 0.02 Gy, and mean left anterior descending coronary artery dose was 0.31 Gy. Her ipsilateral lung V20 was 0%, with a mean dose of 0.21 Gy. There was no dose to contralateral breast. She tolerated her course of treatment very well without acute adverse effects.

Conclusions

Proton partial breast irradiation enables treatment of the left-lower inner quadrant tumor location with excellent sparing of cardiac and lung dose, avoidance of the contralateral breast, and full coverage of the target volume.

References


Factors Associated with Advanced Presentations of Melanoma in the United States from 2004-2015: A
National Cancer Database Analysis

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1University of Florida, Gainesville, FL, USA. 2Mayo Clinic, Jacksonville, FL, USA. 3Penn State Cancer Institute, Hershey, PA, USA

Purpose

Melanoma represents the highest incidence of skin cancer deaths in the United States. Although there have been significant advances in both the diagnosis and treatment of melanoma, the mortality rates remain high and continue to rise. The primary aim of this study is to leverage the National Cancer Database (NCDB) to identify risk factors associated with advanced presentations of malignant melanoma, potentially improving the screening process for melanoma.

Method

Advanced melanoma is defined as AJCC 8th edition Stage III and Stage IV. Patients diagnosed with stage III-IV cutaneous melanoma with appropriate staging and pathologic confirmation from 2004-2015 were selected for analysis. Patient-specific variables were analyzed using chi square and binary logistic regression multivariate analysis to elucidate factors associated with patient presentations of advanced stage melanoma.

Results

A total of 477,914 patients met the inclusion criteria and 63,291 presented with advanced disease. Factors associated with presentations of advanced melanoma included lower income, Medicaid insurance or uninsured, far distance from treatment centers, male, younger age, more comorbidities, and Southeast location (p < 0.05 for all). All factors were confirmed to be significant on multivariate analysis (p < 0.05 for all).

Conclusions

Age, gender, race/ethnicity, geographical location, socioeconomic factors, and distance to treatment center all contribute to differences in diagnosis. In order to improve melanoma screening and education, medical providers, epidemiologists, and government organizations should be aware of the factors associated with advanced presentations of melanoma in order to improve the rapid diagnosis and treatment in order to reduce mortality in a curable disease.

Categories

Clinical investigations

Risk of Intracranial Failure with Stereotactic Radiosurgery for Extensive-Stage Small Cell Lung Cancer Brain Metastases

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Purpose

Small cell lung cancer (SCLC) is considered a systemic disease associated with diffuse spread to brain, which drives the rationale behind the current paradigm of whole brain radiotherapy (WBRT) over stereotactic radiosurgery (SRS) when treating patients with extensive stage (ES)-SCLC with brain metastases (BM). However, with the availability of three-dimensional or thin-slice magnetic resonance imaging (MRI) capable of detecting even small lesions, we are re-evaluating whether stereotactic radiosurgery is an appropriate option in brain management in untreated patients with limited spread to brain and in the management of progressive disease after prior prophylactic cranial radiation (PCI) or WBRT. We report on our experience over the past decade with ES-SCLC BM treated with SRS at our institution.

Method

Patients with BM secondary to ES-SCLC cancer that were treated with SRS from 2011 to 2019 were retrospectively reviewed. Clinical demographics and radiation treatment parameters were investigated to identify risks of local failure and distant brain failure with SRS.

Results

Fifteen (15) patients with ES-SCLC were treated with SRS for 74 total BM, and median clinical follow-up (FUP) was 5.4 months (0.0 – 38.9 mo.). Extracranial metastases were present in 9 patients at time of SRS. Prior to SRS, PCI had been administered for 55 BM in 9 patients, therapeutic WBRT for 4 BM in 1 patient, while 8 BM had received both for 1 patient. Median number of BM treated for each patient with SRS was 4 with a median prescription dose of 18.0 Gy. Of 32 BM with radiographic FUP longer than a month, there were 9 local failures (LF; 28.1 %) with a median of 5.2 mo. to LF.
(3.7 – 17.6 mo). 7 patients had distant brain failure (DBF) after SRS with a median of 10.4 mo to DBF from first SRS treatment, with some patients demonstrating long-term freedom from DBF (2.4 - 30.5 mo). Median overall survival (OS) was 6.51 mo. with the probability of survival at 6 and 12 mo. being 60 % and 22.5 %, respectively. Long-term survival was possible with salvage SRS after prior PCI with two patients surviving 32.4 and 38.9 mo. after SRS, respectively. Both patients had prior PCI and no extracranial disease at time of first SRS, and were successfully salvaged multiple times with SRS subsequently for cases of local and distant failure.

Conclusions

We report on a single institution’s experience treating a cohort of ES-SCLC patients, mainly in patients treated with prior brain irradiation, who received SRS as salvage therapy. Survival outcome and brain control appeared similar to use of repeat whole brain radiotherapy, while sparing the patients the potential neurocognitive risks of PCI or WBRT. More investigation is warranted for the use of SRS in management of SCLC brain metastasis under various clinical circumstances.

Categories

Clinical investigations

Comparing Patient and Physician Reported Toxicity After High Dose Rate Prostate Brachytherapy In Patients Receiving Two Implants Separated by a One-Week Interval

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Purpose

Hypofractionated high dose rate (HDR) brachytherapy (BT) as monotherapy has been shown to be a safe and effective method of treating men with low and intermediate risk prostate cancer. Different series have used varying lengths of time between treatments. There are limited data studying the influence of the time between treatment on treatment-related toxicity. This study aims to assess if the timing between HDR treatments has an impact on patient and physician reported toxicity.

Method

All patients were treated on a prospectively maintained institutional IRB-approved database. Patients were treated with HDR-BT as monotherapy with 13.5 Gy x 2 fractions, given as one fraction per implant, performed 1-2 weeks apart based on patient preference and operating room availability. Patients receiving their two factions within 10 days represented the one-week cohort, while those receiving treatment with 11 days or more between implants represented the two-week cohort. Patient reported urinary, bowel, and sexual function were assessed using the IPSS and EPIC-26 tools. These values were collected before BT and at regular follow-up visits. Physician reported toxicity was assessed utilizing CTCAE v5.0 criteria and collected at each follow-up visit. Univariate and multivariable analysis with linear regression and chi-squared testing were used to assess for differences in baseline characteristics. Linear mixed effects models were used to compare patients and physician reported toxicity over time based on their implant interval duration.

Results

Results from 127 patients were analyzed, with 67 patients treated within one week, and 60 patients treated over two weeks. Median follow-up was 18 months. The two week treatment cohorts had a higher baseline mean PSA (8.26 vs 6.44, p=0.01) and EPIC-26 Bowel score (97.58 vs. 91.9, p=0.017). There were no other difference between the groups in baseline demographic, oncologic, or patient reported toxicity variables on univariate or multivariable analysis. Over time, there were no difference in the patient or physician reported toxicities between the two groups. Grade 2 GU toxicity was observed in 69% of cases, with no difference between the one and two week groups (70% vs 68%, p=0.825). There was a single episode of Grade 3 GU and sexual toxicity reported, with no Grade 4 or 5 toxicities. There were no statically significant difference in the rates of acute urinary retention between the one and two week cohorts (5 events vs 1 event, p=0.124).

Conclusions

The duration between treatments for patients undergoing HDR BT as monotherapy for prostate cancer using a two implant regimen does not appear to be associated with differences in patient-reported or physician-graded toxicities or rates of acute urinary retention. A
A retrospective analysis of image guided radiotherapy for prostate cancer: rectal dosimetric consequences of different alignment paradigms

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Purpose

Two different in-room alignment procedures in prostate radiotherapy indicate distinct paradigms: (a) always maximize target dose (e.g. by aligning intraprostatic fiducials, “F”) or (b) always minimize the rectal dose (e.g. by matching the prostate-rectal interface (PRI) via cone beam computed tomography (CBCT), “PRI”). We reviewed our institution’s “PRI” and “F” alignments via CBCT to estimate the relative rectal dosimetric differences between the two setup conditions.

Method

Daily CBCTs from a cohort of 8 patients with intraprostatic fiducials were aligned with simulation CTs using both “F” and “PRI” strategies. The rectal doses received in each scenario were estimated by contouring rectums on all CBCTs and rigidly mapping the planning dose on each daily CBCT according to the respective shift alignment. The rectal volume (cc) receiving at least 40 Gy (V40) was computed and compared between “F” and “PRI” strategies. The relative comparison of daily V40 for the two alignment scenarios characterized the effectiveness of the “PRI” vs “F” alignment with respect to the rectal sparing. The comparison of the planning and daily V40 indicates whether the simulation anatomy was a good representation of the daily anatomy. In addition, the necessary shifts from “F” to achieve the “PRI” alignment were evaluated. The percentage number of fractions that the magnitude of the shift was larger than PTV margin (indicating potential target underdosage) was calculated. The percentage number of fractions that “PRI” alignment moved the rectum closer to high isodose regions were also calculated.

Results

The average rectal V40 over all patients and fractions was less in the “PRI” paradigm compared to the “F” paradigm (15.8cc vs. 17.6cc). The rectal dosimetric differences between “PRI” and “F” paradigms were smaller than the dosimetric differences between “PRI” and simulation plan on average by 21.1%. It was found that 25% (2/8) of the cases investigated had a reproducible daily anatomy compared to the CT simulation planning anatomy. The remaining 62.5% (6/8) cases had less reproducible setup. Of this group, 3 patients had dosimetrically favorable setup alignments while 3 had unfavorable setup alignments. Over all patients and all fractions, 18.9% (range 0-62.5%) of the shifts from “F” to “PRI” were larger than the PTV margin. The “PRI” alignment resulted in an increase of rectal V40Gy over the “F” scenario in 37.3% (range 12.5-47.6%).

Conclusions

The difference in rectal sparing between “F” and “PRI” paradigms are likely irrelevant clinically, and much less than the difference from the CT simulation anatomy. In addition, the potential benefit of “PRI” alignment is undercut by shifts that bring the rectum closer to the radiation field. These findings may have much more detrimental consequences in hypo-fractionated treatments.
the rising popularity of these sites, there is ease access for the public to evaluate and rate physicians. We surveyed practicing radiation oncologists from the American Society of Radiation Oncology (ASTRO) to better understand how physicians perceived the online assessments at these sites and their effect on physician burnout.

Method

An online survey was delivered to 6,199 practicing radiation oncologists worldwide. The survey consisted of 14 questions that addressed radiation oncologists' awareness and perceptions of internet rating sites. In this study, we focus on negative feedback and its potential effects on providers. Chi-square testing, chi-square goodness of fit, and generalized linear models were used to compare the variables. Statistical significance of alpha level was determined using a priori criteria p<0.05. This study was approved by our IRB.

Results

Negative Feedback & Challenging a Review

Of the 6,199 physicians originally solicited, 447 (7.2%) responded. Of those, 159 (35.6%) received what they perceived as negative feedback. The majority, 133 (83.6%) did not challenge the online review. The 26 (16%) respondents who did challenge an online review were significantly more likely to have received negative feedback (p-value<0.001) and to personally review their own online feedback (p value=0.044) than those who did not challenge.

Burnout

Of the 447 respondents, 154 (35%) agree and 46 (10%) strongly agree that virtual patient assessments contribute to burnout, while 39 (9%) disagree and 6 (1%) strongly disagree. Using the chi-square goodness of fit test, we conclude the distribution is asymmetric (more agrees than disagrees), with p-value less than 0.001 (p < 0.001). In addition, the estimated proportion of ‘agrees’ is 45.31%, with 95% exact binomial confidence interval [40.57%, 50.11%] and ‘disagrees’ 10.30%, with 95% exact [CI 7.61%, 13.54%]. Thus, we observe that there is no overlap of these two confidence intervals. Therefore, we are able to conclude the asymmetry of the distribution. Among surveyed radiation oncologists, actively reviewing one’s own feedback (p-value = 0.46), increased frequency of reviewing (p-value = 0.25), and receiving negative feedback (p-value = 0.25) were not found to be significantly correlated with the belief that virtual healthcare reviews contribute to burnout.

Conclusions

Regardless of receiving negative feedback, physicians perceived virtual internet patient assessments to contribute to burnout. As internet assessment tools become more prevalent, physicians need to have a high awareness of their public image. Further research needs to be conducted into the public’s perception of their providers and healthcare as it may be influencing their expectations and skew the delivery of care.

Categories

Socioeconomic/ethical issues/health outcomes research

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How Do Patients Spend Their Medical-Expense Financial Grants?

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Purpose

Cancer patients suffer from a significant burden of financial toxicity while undergoing treatment. The goal of our study was to determine financial priorities when patients are given a financial grant for medical expenses.

Method

This study was a retrospective review of a single outpatient community center from January 2019 to August 2019. The study was exempt from IRB review. All treated patients were offered a financial grant for medical expenses regardless of income level. Patients were included in this analysis if they used any portion of the financial grant for medical expenses. Most patients received 500 dollars but funds was offered based on need and/or individual cost. Numbers are reported as mean +/- standard error of the mean.

Results

67 patients were offered the financial grant with 69 unique financial charges. Patients used a mean total of $224.05 +/- $28.57. Categorically, the majority of the grant charges (by total number of charges) were utilized for...
The purpose of this report is to present the case of a patient diagnosed with a squamous cell carcinoma of the base of the tongue, stage II (cT2 cN0 M0) who was treated with primary radiotherapy using a hypofractionated regimen.

Method

This is a case report.

Results

The patient is an 89-year old female who had a one month history of an aphthous ulcer on the left posterior tongue. She sought consult with an otorhinolaryngologist, and underwent a wedge biopsy to evaluate the lesion, revealing a squamous cell carcinoma. A contrast-enhanced CT scan was performed to evaluate the disease extent, which revealed no enlarged lymph nodes. No data on the p16 status was available. The patient was subsequently treated with a hypofractionated, 22-day course of radiotherapy, delivering 66 Gy to the primary site of the tumor and the left oropharyngeal (BED of 85.8 Gy) and 55 Gy (BED of 68.8 Gy) to the cervical nodal regions with suspected subclinical disease. The cervical nodal regions treated included bilateral Level Ib, II, III, and IV. There was complete resolution of the tumor, as documented by post-treatment magnetic resonance imaging. The main acute toxicities included dysphagia, xerostomia, dermatitis, and dysgeusia. All these toxicities, except for dysgeusia, have completely resolved within less than a year after radiotherapy.

Conclusions

Hypofractionated radiation therapy can be considered in elderly patients with early-stage squamous cell carcinoma of the base of the tongue. This case has shown that this can be well-tolerated and can achieve complete radiologic response of the primary tumor, durable for at least a year.

References


Categories

Clinical investigations

A Validation of the Nieder Method for Determining
**Spinal Cord Reirradiation Tolerances**

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**Purpose**

Dr. Carsten Nieder and his colleagues published data on spinal cord reirradiation in 2005 as a guide for radiation myelopathy risk estimation. These data have been used in our clinic to evaluate radiation risk to the spinal cord due to reirradiation and have helped drive clinical decision-making. This research seeks to validate the method for determining risk of radiation myelopathy published by Nieder et al.

**Method**

The tolerance for the spinal cord is well known in the field of Radiation Oncology; however, the concept of radiation forgiveness over time is still being studied. In our clinic, a large percentage of patients have previously been treated with radiation. When there is overlap of previous and intended targets, additional steps are taken to evaluate the efficacy and safety of the treatment. In areas containing the spine, the method proposed by Carsten Nieder, et al. in 2005 and updated in 2006 is used to evaluate dose to the spinal cord. Nieder uses 3 factors for determining risk: time since previous radiation, total biologically effective dose (BED) to the spinal cord, and the BED for each individual course of radiation. These parameters allow each to be categorized as low, intermediate, or high risk of radiation myelopathy.

**Results**

Of the approximately 150 cases of spinal cord retreatments performed at our clinic between 2015 and 2018, 25 were determined viable for this study. Patients were excluded from the study if they did not have direct overlap between treatments or lacked sufficient follow-up data (i.e., deceased shortly after treatment, left clinic, etc.).

Of the 25 retreatments that were evaluated, 24% were retreated within 6-9 months of the original treatment, 40% were treated within 10-24 months, and 36% were treated greater than 24 months after the original treatment. All cases except 1 fell in the low risk category (<150.0 cumulative BED). In this particular case the patient was receiving a third course of treatment to the t-spine. The BED for each course was less than 90 Gy2, with a cumulative BED of 162.6 Gy2 from all three courses. The time interval between the first and second course was 29 months, and 45 months between the second and current.

These reirradiation treatments were delivered with various fractionation schemes including 8% in a single fraction, 8% in 3 fractions, 12% in 4 fractions, 44% in 5 fractions, 12% in 8 fractions, and 16% in greater than 20 fractions.

In 25 cases of spinal cord reirradiation between 2015 and 2018, none of the patients treated in our clinic have had any incidence of radiation myelopathy.

**Conclusions**

Our clinic utilizes the Nieder method to determine appropriate dose levels in reirradiation, and, to date, the method has been proven effective.

**Categories**

Clinical investigations

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**The Response Rate of Ovarian Cancer Central Nervous System Metastases to Palliative Radiotherapy**

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**Purpose**

The central nervous system (CNS) is a rare site of metastasis for women with ovarian cancer (2.1% incidence). As only ~600 cases have been reported, clinical outcomes are not robustly documented. We sought to report the response rates of a large series of such women treated with palliative radiotherapy (RT) in the era of modern systemic agents.

**Method**

A retrospective review was conducted of women with metastatic ovarian cancer treated with palliative RT in our institutional cancer patient database from 2007-2019. Clinical characteristics and outcomes [including partial response (PR), complete response (CR), stable disease (SD), progressive disease (PD), and
overall response rate (ORR)] were analyzed in those with CNS metastases.

**Results**

47 courses of CNS-directed RT were delivered to 32 women (median age 63). 81.3% had high grade serous histology. Indications for RT included neurologic symptoms/pain (36.2%) and oligometastatic/oligoprogressive disease (OG) (63.8%). All treatment courses were delivered with prior or concurrent taxol- (34.0%), platinum- (25.5%), doxorubicin- (14.9%), bevacizumab- (14.9%), or PARP inhibitor-based (8.5%) systemic regimens.

The most common RT techniques included stereotactic radiosurgery (SRS, 57.4%) and 2D/3D (21.3%). 92.6% of SRS treatments were Gamma Knife. Non-SRS prescribed doses ranged from 20-41.4 Gy in 5-23 fractions (most commonly 30 Gy/10 fractions, 40%). SRS doses ranged from 15-21 Gy in 1-5 fractions. The ORR (CR+PR) of 33 evaluable courses was 69.7% (58.3% in non-SRS RT courses, and 76.2% in SRS courses).

Specifically, of 7 non-SRS courses for clinical symptoms, the ORR (PR+CR) was 57.1% (1 CR >3 months, 2 PR >3 months, 1 PR <3 months, 3 PD in <1 month). Of 4 SRS courses for clinical symptoms, the ORR of the index lesion was 75% (1 CR >3 months, 2 PR <3 months, 1 PD in <3 months). Of 5 non-SRS RT courses delivered to OG, the ORR was 60% (1 CR >3 months, 2 PR >3 months, 2 with SD >3 months). Of 17 SRS courses delivered to OG, the ORR of the index lesion was 76.5% [11 CR >3 months, 1 CR <1 month (unevaluable thereafter), 1 PR >3 months, 4 with SD >3 months].

**Conclusions**

Palliative radiotherapy is a reasonable option in the setting of symptomatic or oligometastatic/oligoprogressive CNS metastases from ovarian cancer in the era of modern systemic agents. Higher dose-per-fraction SRS may confer more durable and improved response rates in index lesions compared to conventional palliative regimens. Given the limited life expectancy associated with this diagnosis, prospective data investigating the optimal radiotherapy technique and schedule is warranted.

**References**


**Categories**

Clinical investigations

**43**

A Decade of Innovation in the Field of Brachytherapy: An Analysis of United States Patents

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**Purpose**

Brachytherapy was invented over a century ago. Arrived at separately by Pierre Curie and Alexander Bell in the early 1900s, this idea took hold of the oncology world and altered the landscape of cancer therapy.¹ Innovation in the field of brachytherapy has continued, and inventors often seek patent approval for these advancements. We sought to analyze trends in brachytherapy innovation based on brachytherapy-related patents awarded in the past decade in order to provide insights that will help inform future research and entrepreneurship in the field.

**Method**

The United States Patent and Trademark Office (USPTO) database was searched for patents awarded between January 1st, 2009 and December 31st, 2018 with a classification code corresponding to the broadest brachytherapy search category. Patent characteristics were recorded to include patent file number, title, abstract, file date, award date, country of assignee, affiliation of assignee, and the number of inventors. Assignee affiliation was classified as individual, industry, academic, or combination of industry-academia. Two reviewers classified the theme of invention in each patent based on title and abstract claim of assignee; differences were resolved with consensus. Frequency of themes was assessed overall, and differences between academic, industry, and individual assignee themes were analyzed. Institutional review board approval was not needed as all information was publicly available online.

**Results**

A total of 202 brachytherapy-related patents were awarded by the USPTO
within a ten-year span. Among these, 15% had 1 inventor, 26% had 2 inventors, and 23% had 3 inventors. The mean interval between patents being filed and awarded was 344 ± 283 days (range: 102-1,843 days). The most common countries of patents’ first assignee were the United States (75%), followed by the Netherlands (6%), Germany (5%), and Canada (3%). Within the United States, the largest number of patents was assigned to California (32%), followed by New Jersey (17.9%), Minnesota (5.3%), and Arizona (5.3%). Patents had an industry affiliation in 76% of cases, while 11% were characterized by an academic affiliation, and 5% resulted from collaborations between the two. The three most common themes overall were treatment delivery (19.3%, n = 39), exogenous agents (15.8%, n = 32), and radiation source (9.4%, n = 19). These top themes were similar for U.S. and industry-affiliated patents; however, academic patents had a distinct focus with exogenous agents (27.3%, n = 6), treatment planning (22.7%, n = 5), and radiation dosing (13.6%, n = 3) predominating as the three most common themes.

Conclusions

Patents from industry and academia had differing leading themes, and minimal collaboration was observed. Brachytherapy innovation through patent production in the past decade has been led by the United States and industry inventors.

References


Categories

Socioeconomic/ethical issues/health outcomes research

Use of Machine Learning to Differentiate Residual Tumor from Radiation Changes in Head and Neck Cancer Patients Treated with Definitive Chemoradiotherapy.

Toms Vengaloor Thomas, Edward Florez, Seth Lirette, Ali-Fatem Ardekani
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Purpose

Surveillance imaging for head and neck cancer patients treated with definitive chemoradiotherapy has difficulty in differentiating residual disease from radiation changes or inflammation. Early detection of the residual disease is particularly crucial as those patients have poor outcomes if not treated aggressively. On the other hand, these shortcomings in the imaging might lead to unnecessary interventions, including salvage surgery in patients without the residual disease. This study assessed the use of machine learning models to differentiate residual disease from radiation changes using radiomics features extracted from surveillance CT and PET scans.

Method

A HIPPA-compliant, IRB-approved retrospective posthoc analysis of patients with head and neck treated with definitive chemoradiotherapy was performed. From them, 25 patients reported having a residual disease on the first surveillance CT soft tissue of the neck (at two months after chemoradiation) were selected. The information regarding further follow up imaging, salvage surgery with pathology, and long-term outcomes were collected.

All gross tumor volumes (GTVs) were transferred from the treatment planning CT scan to a DICOM viewer (MIM® MaestroTM Software Inc., v6.7.10). Then, a radiation oncologist contoured the residual lesions in the two months follow up CT (GTV post-CT) and three months follow up PET scan (GTV post PET/CT) through MIM’s tools. Next, GTVs were exported to MatLab® using an extension written in Java, which was incorporated into MIM. Then, radiomic features were extracted from each tumor through quantitative in-house MatLab algorithms using different approaches without normalization. Finally, neural network machine learning models were constructed to predict (1) residual tumor from PET/CT radiomics (2) residual tumor from CT radiomics (3) positive PET/CT findings from CT radiomics.

Results

Each of the 250 radiomics features without normalization was used to construct the neural network models. The model using PET/CT radiomic features was able to differentiate residual tumor from radiation changes had a modest discriminative ability (AUC =0.69). Predicting residual tumor from CT radiomic features was not successful (AUC=0.52). The model to predict positive PET/CT findings from CT soft tissue neck had a reasonable discriminative ability (AUC =0.70).

Conclusions
A machine learning model using PET/CT radiomic features was able to differentiate residual tumor from radiation changes in a small group of head and neck cancer patients treated with definitive chemoradiotherapy. This model could be used to identify patients with a high probability of residual disease, which needs aggressive salvage surgery while preventing other patients with radiation changes or inflammation to avoid unnecessary treatment and associated morbidity. This model needs to be validated in a larger cohort of patients before a generalized use.

References

Categories
Physic 47

Current Use of Stereotactic Body Radiation Therapy for Low and Intermediate Risk Prostate Cancer: A National Cancer Database Analysis
Timothy Malouff, William Stross, Danushka Seneviratne, Mark Waddle, Byron May, Steven Buskirk, Katherine Tzou
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Purpose
Recent studies have demonstrated both safety and efficacy of stereotactic body radiation therapy (SBRT) as monotherapy in the treatment of low- and intermediate risk prostate cancer. This study serves as an update for analyzing trends in SBRT compared to conventional and hypofractionated regimens in the United States over the past decade.

Method
This retrospective review was conducted using the National Cancer Database. We identified 114,931 patients with sufficient diagnostic and treatment information treated with definitive radiation therapy in the United States from 2004 to 2015. The relative utilization of conventional fractionation (defined as 180-200 cGy per fraction and >5 fractions), moderate hypofractionation (defined as >200 cGy per fraction and >5 fractions), and SBRT (defined as >200 cGy per fraction and 5 fractions or less) were compared over the same time period. Logistic regression models were used to estimate trends. Demographic factors were collected and analyzed using chi-squared tests and independent t-tests.

Results
The proportion of prostate cancer patients receiving SBRT increased substantially from 0.9% in 2004 to 19.5% in 2015. Moderate hypofractionation exhibited some growth, increasing from 2.7% of patients to 4.7% in 2015. Conventional fractionation use declined significantly from 96.3% in 2004 to 75.8% in 2015. Notably, there was a sharp decline in the absolute number of patients receiving conventional fractionation in 2011, from 14,699 patients treated in 2009 to 1492 in 2011. Patients treated with SBRT were more likely to be treated in academic centers, younger, and have higher income than other fractionation groups. The most frequently used fractionation schedule was 3625 cGy in 5 fractions.

Conclusions
The use of SBRT for low- and intermediate-risk prostate cancer has increased significantly from 2004 to 2015, coinciding with recently published data supporting the efficacy and favorable toxicity profile of this technique.

Categories
Socioeconomic/ethical issues/health outcomes research 48

Assessment of Contouring Practices and eContour Usage Among US Radiation Oncologists: A Mixed Methods Study
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Purpose
Contour delineation is an integral part of the radiation treatment planning process which can impact patient outcomes. Accurate contours are critical for maximal local disease control with minimal tissue toxicity. While there are multiple contouring aids and established peer review
processes, significant discrepancies in contouring practices remain across the United States. This study aims to better understand current contouring-related strategies and practices used by US radiation oncologists, focusing on physician- and organizational-level factors that affect the quality of final contours. Secondly, the study will assess the physician-reported clinical impact of eContour, a 3D image-based website designed to improve access to evidence-based contouring information. With over 50% of US radiation oncologists registered as users, we will explore how and why physicians use this resource in order to improve eContour for practicing clinicians.

**Method**

This is a mixed methods study with a sequential explanatory design. Between November 2019 and March 2020, a survey (developed and piloted through informal interviews) will be followed by formal qualitative interviews. A random sample of 500 practicing US radiation oncologists will be recruited from the ACRO database (784 eligible members excluding residents), with adjustments made to purposefully oversample the eContour user subset (goal of n=250) following database cross-referencing. All participants will receive survey questions on demographics, tools used to support contouring, and contouring quality assurance (QA) practices. eContour users will additionally be asked about platform usage, while non-users will provide general impressions of eContour following a brief website introduction. The survey will be sent via sequential mixed modalities to increase response rates. Other strategies will include prenotification, noncontingent incentives, personalized correspondence, providing multiple return options, and including stamped return envelopes. Respondents will be invited post-survey to participate in qualitative interviews that will explore response nuances and quality improvement (QI) tool usability. Interactions will be recorded and transcribed for formal qualitative analyses. Quantitative data (including website analytics) will be analyzed with descriptive statistics, with additional ordinal and multinomial logistic regression analyses to assess underlying influencing factors in relation to survey responses. Quantitative and qualitative data will ultimately be integrated during analysis for significance enhancement.

**Results**

Informal interviews (n=7) were conducted to inform survey development, with questions exploring contouring strategies. Participants identified multiple barriers to using contouring-related resources, including a lack of online library access in community practices, and a perceived need to improve peer review processes. Survey questions were developed accordingly. The study is ongoing. Survey results and website analytics will be presented at the conference.

**Conclusions**

Findings may provide greater insight regarding contouring strategies employed by US radiation oncologists, highlighting potential needs and obstacles that perpetuate discrepancies in the field. This will guide further development of contouring-related QI tools (including eContour) and implementation strategies.

**Categories**

Translational science

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**Neurologic Outcomes of Stereotactic Radiosurgery for Brainstem Metastasis**

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**Purpose**

Brainstem metastases (BSM) constitute 5% of all brain metastases, but can cause great morbidity and mortality. Stereotactic radiosurgery (SRS) is not widely used due to postulated radiosensitivity of the brainstem. The goal of this study is to review the safety and efficacy of hypofractionated SRS for BSM.

**Method**

Patients with BSM treated with SRS at a single institution between 2009 and 2019 were retrospectively reviewed. Toxicity was defined according to the Common Terminology Criteria for Adverse Events (CTCAE 5.0). Probit normal tissue complication probability (NTCP) models for brainstem were constructed assuming \(\alpha/\beta\) of 2 for late effect.

**Results**

A total of 57 patients with 71 brainstem lesions were included. The most frequent primary histologies were non-small cell lung cancer (47%) and melanoma (14%). Twelve (21%) patients received whole brain radiotherapy (WBRT) prior to SRS for...
BSM. Ten patients (18%) had more than one brainstem lesion (range 2-4) treated during the same SRS course, and 46 (81%) had more than 1 brain metastases treated during the same SRS course. Forty two patients (72%) received systemic therapy within 1 month of SRS, of whom 16 (28%) received immunotherapy. The median survival after brainstem SRS was 4.2 months. With a median imaging follow up of 7.1 months, the overall local control rate was 87%.

The majority of lesions were treated over a hypofractionated course of 25Gy in 5 fractions. Eight lesions received 15-16Gy in 1 fraction, and 16 were treated with a median of 22.5Gy in 3 fractions. The median prescription isodose line was 85%, and median planning target volume was 0.36cm³ (0.04-16.28cm³). The median 1-fraction equivalent dose of brainstem maximum was 13.8Gy (10.2-14.9Gy).

No grade 4 or 5 toxicity was observed. Eleven patients (19%) required increased dose of steroids (grade 2), and only 1 patient was briefly hospitalized for vertigo and headache 5.3 months after SRS (grade 3). Prior WBRT, receipt of immunotherapy or brainstem maximum dose were not associated with higher risk of grade 2-3 toxicity. The average daily dexamethasone dose was 3.7mg prior to SRS, 3.3mg 1 month after SRS, and 1.3mg 3 months after SRS (p=0.008 vs pre-SRS). At 3 months, 82% of patients were not on any steroids. NTCP modeling of patients treated between 2009 and 2017 showed a strong correlation between post-SRS toxicity with radiation dose to 1cm³, 5cm³ and 10% of the brainstem volume (D1cc, D5cc, D10%).

Conclusions

SRS may provide durable local control and symptomatic relief for metastases in the brainstem. The majority of patients were able to discontinue steroid after SRS for BSM. There may be a dose-volume relationship between irradiated brainstem and post-SRS complications. Further studies are needed to delineate dose constraints for safe SRS to the brainstem.

Categories

Clinical investigations

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The Geographic Density of Radiation Oncologists in the United States

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Purpose

Radiation oncology, more so than any other field in medicine, is heavily geographically dependent, due to the nature of fractionated radiotherapy administered from expensive and immobile equipment. As such, the geographic distribution of radiation oncologists (RO) throughout the United States significantly impacts access to care. We aimed to describe the geographic distribution of practicing RO using publicly available data.

Method

The number of practicing radiation oncologists and total population in each county in the United States was ascertained from the 2017 Area Health Resource File (AHRF) published by the Health Resources & Services Administration. We then calculated the number of practicing radiation oncologists per 100,000 people (RO/100,000) and describe this for various populations.

Results

In 2017, 5,338 practicing radiation oncologists were recorded in the AHRF serving a population of 326.1 million Americans, thus nationwide there are 1.6 RO/100,000. Counties in urban areas of >1,000,000 people have 1.9 RO/100,000; this is higher than counties in urban areas <1,000,000 people (1.6 RO/100,000) or non-urban counties (0.6 RO/100,000). Counties with a median household income above the approximate national median ($60,000) had a slightly higher RO/100,000 than those below it (1.8 vs 1.5). Of the four Census-defined regions, the Northeast has the highest RO/100,000 at 2.1 compared to the Midwest (1.7), South (1.5), or West (1.5). Table 1 shows the RO/100,000 by state ranked from highest to lowest.

Table 1. Radiation oncologists per capita by state

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<th>State</th>
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<td>Massachusetts</td>
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<td>New Mexico</td>
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Conclusions

There is some geographic inequity in the distribution of practicing radiation oncologists in the United States. The Northeast, large urban centers, and wealthier counties have a higher number of RO/100,000 than other areas. We urge further study into the clinical implications of these inequities.

Method

All pediatric brain tumor (age ≤ 21 years) patients treated at our institution with radiation therapy between 2004 and 2018 were reviewed with IRB approval. 142 patients were identified. 85 of them had more than 6 months of follow-up and were included for further evaluation (28 proton, 53 photon, 4 both). The diagnosis, surgical history, chemotherapy, radiation modality, dose, and fractionation were reviewed for all patients.

RN was determined by reviewing symptoms and imaging findings after radiation when progressive disease was excluded. Common RN treatments (hyperbaric oxygen, steroid and/or bevacizumab administration) were also reviewed.

We also observed that CM was common after radiation therapy. All patients with at least a year follow-up were reviewed for CM. 69 patients were identified (24 proton, 42 photon, 3 both). These were defined as radiographically determined CM that arose after radiation therapy.

We compared the results for RN and CM using two proportion Z-test.

Results

The median post-treatment follow-up was 39.7 months. 2 of the 28 proton (7.1%) patients and 4 of the 53 photon (7.5%) patients had radiographic radiation necrosis (p 0.986). Both (7.1%) of the proton patients and half (3.8%) of the photon patients were symptomatic (seizures, focal neurological deficits). None of the patients that had both modalities had...
RN. The median time to necrosis after radiation therapy was 7.8 months. There were no deaths due to RN. In 5 out of 6 cases, there were areas identified for improvement with dose/fractionation and organ at risk (OAR) constraints.

2 (8.33%) proton and 7 (16.67%) photon patients had CM after radiation therapy (p 0.343). One CM patient had both modalities of treatment. The median time from radiation therapy to CM formation was 55 months.

Conclusions

Our retrospective review of all brain tumor patients treated with proton or photon radiation showed no significant difference in RN between modalities. Furthermore, radiographically determined cavernous malformations were similar in both cohorts. The review of the cases with RN supports the stringent adherence to standard-of-care radiation fractionation and dose constraints.

Radiotherapy for CNS Myeloma: A Single-Institution Experience

<table>
<thead>
<tr>
<th>Patient</th>
<th>Central nervous system disease</th>
<th>RT Fields</th>
<th>Dose (Gy)/fractions</th>
<th>Clinical Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LM</td>
<td>CSI</td>
<td>4/2 (planned for CSI)</td>
<td>ND</td>
</tr>
<tr>
<td>2</td>
<td>LM &amp; BM</td>
<td>CSI</td>
<td>4/2 (incomplete)</td>
<td>ND</td>
</tr>
<tr>
<td>3</td>
<td>LM</td>
<td>WBRT</td>
<td>30/10</td>
<td>NR</td>
</tr>
<tr>
<td>4</td>
<td>LM</td>
<td>WBRT</td>
<td>25/10</td>
<td>NR</td>
</tr>
<tr>
<td>5</td>
<td>LM</td>
<td>Left orbit &amp; sella</td>
<td>20/8</td>
<td>NR</td>
</tr>
<tr>
<td>6</td>
<td>LM</td>
<td>Left orbit</td>
<td>25.2/14</td>
<td>PR</td>
</tr>
<tr>
<td>7</td>
<td>BM</td>
<td>Right temporal lobe</td>
<td>20/5</td>
<td>NR</td>
</tr>
<tr>
<td>8</td>
<td>BM</td>
<td>Bilateral frontal lobes</td>
<td>21/7</td>
<td>ND</td>
</tr>
</tbody>
</table>

Results

9 patients were treated with 10 RT courses. Median age at treatment was 61 (range, 41-69). 7/9 diagnoses were established by MRI with parenchymal/meningeal metastases, 1 by MRI with cranial nerve invasion, and 1 by exam demonstrating choroidal metastasis. RT details are in Table 1. Prescriptions ranged from 4-30 Gy, including 1 completed 4 Gy course (planned for craniospinal RT at an outside institution), and 1 incomplete 4 Gy course who enrolled in hospice and stopped treatment early. Median dose per fraction was 2.5 Gy (range, 1.8-4). Treated fields included whole brain, craniospinal, orbit, partial brain, and base of skull with retreatment to a matched whole brain field. 3/10 courses had documented clinical response, all partial. All patients died with median survival (end of treatment to death) of 79 days (range, 10-151).
Patients with CNS myeloma have poor prognosis. Based on our small series, palliative cranial RT does not yield a clinical response for most patients. Therefore, best supportive care may be reasonable management in many cases. If treating with RT, hypofractionated courses should be considered. Early termination of RT is reasonable for patients with clinical benefit opting to discontinue RT in favor of best supportive care.

**References**


**Categories**

Clinical investigations

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**Evaluation of the Use of Standardized Simulation Order Templates to Improve Guideline Adherence**

Resident Joseph A Jones, Resident Ashlyn S Everett, Director of Operations Ginna Blaylock, Attending Drexell H Boggs

University of Alabama at Birmingham, Birmingham, AL, USA

**Purpose**

The application of process improvement methodologies, including Lean and Six Sigma, have demonstrated improvement in critical-to-quality metrics across multiple industries and are becoming increasingly necessary in healthcare to reduce costs and error. Site-specific guidelines were developed in our department to standardize specific requirements for simulation, planning, and treatment across multiple providers and sites. Simulation order templates for each site were created to improve standardization and compliance to guideline requirements. The purpose of the current study is to demonstrate the use of simulation order templates to reduce errors and variability associated with simulation.

**Method**

As part of a pilot audit, 196 patients with breast cancer requiring adjuvant radiotherapy at our institution from 4/10/2017 to 3/26/2019 were evaluated. Based on department breast guidelines, adherence to the following factors were assessed: patient position, immobilization method, marker placement for scar and breast borders, and presence or absence of gating. Of note, simulation order data extraction from Cerner did not allow evaluation of presence of gating on pre-template orders and that feature was not included in the analysis. A total of 89 and 107 breast cancer patients were evaluated pre- and post-template implementation, respectively, to establish baseline compliance and to evaluate template effectiveness in improving guideline adherence.

**Results**

Prior to template implementation, instructions regarding immobilization requirements and marker placement were added manually in 11 individual fields, which resulted in an increase in error rates and variability. With the creation of simulation order templates, fields were pre-populated to include standard position, immobilization and marker placement. There were 534 opportunities for error in the pre-template population and a total of 188 errors noted, yielding a guideline compliance rate of 64.8 ± 16%. There were 749 opportunities for error in the post-template population and 134 errors noted, yielding a guideline compliance rate of 82.1 ± 10%. Pareto analysis of the errors associated with the pre-template population showed that the primary drivers towards non-compliance were the absence of Knee Fix request (46% of errors) and absence of surgical scar marker request (25% of errors). The primary driver of non-compliance in the post-template population was the absence of Knee fix request (86% of errors).

**Conclusions**

Based on the data generated at our institution, the implementation of
simulation order templates aid in compliance to site-specific guidelines and act to reduce variability in meeting simulation requirements. In addition to the improvement in guideline compliance and reduction in variability, it is recommended that a mechanism for routine analysis of guideline adherence be generated to monitor for common errors and enable adjustment in real time to improve compliance.

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Clinical investigations

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Acute Patient-Reported Rectal Bleeding with the Combination of Prostate External Beam Radiation, Brachytherapy Boost, and SpaceOAR®

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1UPMC Hillman Cancer Center, Department of Radiation Oncology, Pittsburgh, PA, USA. 2University of Pittsburgh Medical Center, Department of Urology, Pittsburgh, PA, USA

Purpose
LDR-brachytherapy (LDR-BT) after external beam radiation (EBRT) in intermediate- or high-risk prostate cancer improves outcomes but increases gastrointestinal toxicity versus EBRT alone. A review of LDR-BT at our institution showed acute patient-reported clinically-significant rectal bleeding within 6 months of LDR-BT predicted for late rectal bleeding (HR 3.1, 95% confidence interval [CI] 1.8-5.5) and late bother from bleeding (HR 2.5, 95% CI 1.5-4.4) (1). At our institution, SpaceOAR® is used with LDR-BT after EBRT to reduce rectal dose. Herein, we report acute patient-reported rectal bleeding and bother from bleeding in these patients.

Method
A retrospective review of patients treated with pelvic EBRT (45 Gy/25 fractions), Cesium-131 LDR-BT (85 Gy), and SpaceOAR was conducted. Rectal dosimetry was evaluated on CT the day of LDR-BT. Expanded Prostate Cancer Index Composite (EPIC) surveys were collected pre-BT, two weeks after BT, every three months for year one, and every six months for year two. Patient-reported acute (<6 months post-BT) rectal bleeding and bother from bleeding was collected. Clinically-significant rectal bleeding was defined as occurring more than “rarely” (“about half the time,” “usually,” or “always”), and clinically-significant bleeding bother was defined as considering rectal bleeding a “small, moderate, or big problem.” Severe rectal bleeding was defined as occurring “usually” or “always,” and severe bleeding bother was defined as being a “moderate or big problem.”

Results
Sixty-nine patients treated with EBRT+LDR-BT and SpaceOAR with available EPIC surveys within 6 months after LDR-BT were identified. Median rectal V100%, V75%, V50%, V25%, D2cc, and D1cc were 0.0 (IQR 0-0), 0.0 (IQR 0-0.3), 3.9 cc (IQR 1.7-5.9), 30.2% (24.5-36.7), and 35.0% (27.1-42.0), respectively. Three patients (4.3%) reported acute clinically-significant rectal bleeding, with two patients (2.9%) reporting bleeding as severe. Two patients (2.9%) reported acute clinically-significant bother from bleeding, both described as severe. In all three patients with acute clinically-significant rectal bleeding, bleeding completely resolved six months post-BT.

Conclusions
With the combination of pelvic EBRT, LDR-BT, and SpaceOAR, the rate of acute patient-reported clinically-significant rectal bleeding is low. Further follow-up is needed to confirm the translation of rectum sparing and low rates of acute rectal bleeding to reduced late rectal bleeding with SpaceOAR®.

References
1. Ling DC, et al. Long-Term Patient-Reported Rectal Bleeding and Bowel-Related Quality of Life After Cs-131 Prostate Brachytherapy. Int J Radiat Oncol. 2019;104(3)

Categories
Clinical investigations

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Differences in Nurse, Physician, and Self-Assessed Pain Ratings in Patients Receiving Radiation for Head and Neck Cancer

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University of Alabama at Birmingham, Birmingham, AL, USA
Purpose

Pain is a common symptom among cancer patients and can be related to disease itself or treatment side effects. The most common clinical method to assess pain is the pain intensity numeric rating scale (PI-NRS) which is a 0 to 10 scale typically assessed by a member of the treatment team verbally questioning the patient. Because the PI-NRS is subjective, the recorded rating may vary among providers and may also differ when a self-report form is used. The purpose of this study was to assess for differences in PI-NRS scores between nurses, physicians, and when self-assessed.

Method

The PI-NRS scores for 27 patients with head and neck cancer (HNC) enrolled in a prospective pain management trial (NCT03317730) were reviewed. Pain was assessed at baseline, weekly during radiation, and at the 1- and 3-month follow-up visit. At each encounter, the PI-NRS was typically assessed with a self-report tool (Brief Pain Inventory question 6) and by a nurse or patient care technician. Separate physician PI-NRS were recorded where available. Correlation of PI-NRS by different members of the study/treatment team was assessed using paired samples r and differences in PI-NRS between groups was assessed using non-parametric paired samples testing.

Results

The nurse assessed PI-NRS was available for 260 encounters, self-assessed PI-NRS for 215 encounters, and physician assessed PI-NRS for 91 encounters. For the 207 encounters where both nurse and self-assessed PI-NRS scores were available, the correlation was \( r=0.74 \) (\( p<0.001 \)); the mean nurse PI-NRS was 2.4 (SD: 2.9) as compared to the mean self-assessed PI-NRS of 2.9 (SD: 2.8, \( p=0.001 \)). For the 90 encounters where both nurse and physician PI-NRS scores were available, the correlation was \( r=0.76 \) (\( p<0.001 \)); the mean nurse PI-NRS was 2.6 (SD: 3.0) as compared to the mean physician PI-NRS of 3.2 (SD: 2.8, \( p=0.01 \)). For the 78 encounters where both physician and self-assessed PI-NRS scores were available, the correlation was \( r=0.78 \) (\( p<0.001 \)); the mean physician PI-NRS was 3.2 (SD: 2.8) as compared to the mean self-assessed PI-NRS of 3.0 (SD: 2.6, \( p=0.24 \)).

Conclusions

The PI-NRS is commonly used among practices to quantitatively assess patient pain during head and neck cancer treatments. In this study we observed that nurse reported PI-NRS scores were statistically lower than patient self-assessed and physician PI-NRS score. Self-assessed and physician reported PI-NRS scores were not statistically different. The difference in PI-NRS between providers and when self-assessed should be taken into account when studying pain in cancer patients and physicians should take this into account when assessing pain.

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The Management of Symptomatic Radiation Necrosis After Stereotactic Radiosurgery: Patient Reported Outcomes

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¹Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA.
²Mehmet Ali Aydınlar Acıbadem University, Istanbul, Istanbul, Turkey.
³Mehmet Ali Aydınlar Acıbadem University, Istanbul, Istanbul, USA

Purpose

Stereotactic radiosurgery (SRS) has become an increasingly utilized treatment option in the initial management of patients with brain metastases. Symptomatic radiation necrosis (RN) is a significant treatment related complication which occurs after approximately 10% of treatments. Treatment options for symptomatic RN include surgical resection, steroids, and bevacizumab. We sought to determine the effectiveness of these modalities for treatment of symptomatic RN, based on patient reported outcomes.

Method

We conducted a retrospective review of 217 patients with 414 brain metastases treated with SRS from 2009 to 2018 at our institution. RN was diagnosed according to a combination of criteria, including appearance on serial MRI scans, MR spectroscopy (MRS), and histology. Patients requiring therapy or developing any new neurologic complaints were scored as having symptomatic RN. Response to treatment of symptomatic RN was assessed by the patients during follow ups. Baseline clinical, disease, and treatment related factors were collected.

Results
Symptomatic RN occurred in 26 patients (11%), spread across 50 total lesions (12%). Whole brain radiation was received by 63% of patients either before or after SRS. Median SRS prescription dose was 22 Gy (range, 15-30 Gy) in 1 to 5 fractions. RN most commonly occurred in parietal (40%) and occipital lobes (30%). Eight RN lesions (16%) were treated with steroids with 43% CR and 36% partial response (PR). Fourteen RN lesions (28%) were treated with bevacizumab, resulting in 64% CR and 21% PR. Other than surgery, factors associated with CR on univariate logistic regression included non-lung primary (OR 7.72, 95% CI 1.5-39.4, p=0.014) and age ≥ 54 years (median age 54, range 35-81) (OR 3.54, 95% CI 1.07-11.8, p=0.039).

Conclusions
Surgery is the most effective management option for symptomatic RN followed by bevacizumab with up to 85% response rate. Our results suggest that patient’s age and histology associates with response rate and could help guide treatment decisions for unresectable symptomatic RN.

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Analyzing Patterns of Failure in Patients with Recurrent Glioblastoma after Definitive Treatment

Katherine Grich, Dr. Timothy D. Malouff, Dr. Danushka S. Seneviratne, Dr. Daniel M. Trifiletti, Dr. Jennifer L. Peterson
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Purpose
Glioblastoma multiforme (GBM) accounts for 20% of intracranial tumors and 50% of gliomas. The current treatment paradigm involves maximal safe surgical resection followed by adjuvant chemotherapy and radiation. While tumor recurrence typically occurs within the high dose radiation field, advancements in imaging, radiotherapy technique, and chemotherapy utilization in the past 2 decades may have an influence on this pattern of recurrence. The current study sought to redefine patterns of recurrence in patients with GBM in the modern chemoradiotherapeutic era.

Method
A retrospective review was performed for 23 consecutive patients with recurrent glioblastoma treated from 2012-2018. Clinical and demographic patient information were gathered, including ECOG performance status, IDH-1 mutation status, MGMT status, and types of adjuvant treatment received. At time of tumor progression, MRIs were reviewed to determine if the tumor centroid was within the high dose radiation volume or not. Patient outcomes were recorded and Kaplan-Meier analysis was created to estimate overall survival.

Results
Analysis of demographic factors revealed 74% of patients were male and 52% were over age 60 at the time of diagnosis. IDH-1 wild-type status was observed in 70% of patients and 40% of patients had hypermethylation of the MGMT promoter region. With regard to the treatment received, 29% of patients had a resection, while 58% underwent biopsy only. 96% (22 of the 23 patients) received adjuvant chemoradiation. Our study found 87% of disease recurrences (20 of the 23 patients) occurred in-field. Of the remaining three patients, one experienced progressive disease adjacent to the treatment field and two experienced out-of-field failures.

Conclusions
Our data suggest that despite advancements in diagnostic and therapeutic techniques over recent decades, GBM recurrences still occur within the high dose radiotherapy field. Further research is needed to develop novel therapeutic agents in this disease.

Categories
Clinical investigations

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Efficacy and Toxicity of Stereotactic Proton Ablative Radiotherapy for Primary Tumors and Metastases of the Spine

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Purpose
Analyzing Patterns of Failure in Patients with Recurrent Glioblastoma after Definitive Treatment

Katherine Grich, Dr. Timothy D. Malouff, Dr. Danushka S. Seneviratne, Dr. Daniel M. Trifiletti, Dr. Jennifer L. Peterson
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Purpose
To report the efficacy and toxicity of stereotactic proton ablative radiotherapy (SPAR) for primary tumors and metastases of the spine.

Method

We evaluated all patients receiving ablative proton radiotherapy to tumors of the spine between June 2015 and July 2019. Ablative radiotherapy was defined as 1-5 fractions with fraction size greater than 800 cGy (RBE 1.1). Patients were immobilized with a five-point thermoplastic mask or vac lok, indexed knee cushion, and memory foam. Radiotherapy was delivered via Hitachi PROBEAT-V with either single- or multi-field optimized intensity modulated scanning proton beam. Local control was assessed with MRI, CT, and/or PET-CT. Outcomes were measured from radiation end date to last imaging. Acute and long term adverse events (AE) were assessed based on CTCAE v4.0.

Results

Forty-four patients were treated at 49 unique metastatic spine sites were treated, C-spine (n =2), T-spine (13), L-spine (18), and sacrum (16). Median age was 64. The most common primary histology was prostate. 80% had prior overlapping radiotherapy fields and 20% were retreatment. Patients were treated with a median 3 fractions (range, 1-5) at a median dose of 13 Gy per fraction (range, 10-22 Gy). Median follow up was 22.2 months. Overall survival of 1 and 2 years was 79.1% and 73.8%. Forty-five sites had follow up. The radiographic local control at 1 and 2 years was 74.0% and 56.2%. Local failure free survival at 1 and 2 years was 60.6% and 40.9%. All patients were assessed during and following radiotherapy for acute and long term toxicities. Nine (18%) patients experienced an acute pain flare with four, requiring initiation or increased dose of opioids or steroids for management. Three patients experienced acute grade 1 peripheral sensory neuropathy and 1 patient had acute grade 1 esophagitis. There was one de novo vertebral body compression fracture requiring vertebroplasty and 3 patients with late grade 1-2 sensory peripheral neuropathy.

Conclusions

Stereotactic proton ablative radiotherapy for the treatment of tumors and metastases of the spine is a safe and effective treatment modality, especially in the setting of prior radiotherapy.

Categories

Clinical investigations

Radiation treatment plan evaluation software implementation and breast cancer radiotherapy plan quality

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Purpose

Radiotherapy treatment plan evaluation software allows for specification of dosimetric goals for target coverage and critical structure avoidance, with a visually-appealing presentation of compliance with those goals for a particular radiotherapy plan. One version of this software (ClearCheck by RADformation) was introduced in our health system in April 2018 primarily for standardization of dosimetric parameters across multiple radiotherapy clinic sites and for ease of evaluating treatment plans. Critical structure avoidance has been associated with improved risks, such as the association between major coronary events and mean heart dose (with no apparent threshold) for breast cancer patients1. We therefore secondarily evaluated the effect of software implementation on radiotherapy treatment plan quality for breast cancer.

Method

Forty consecutive breast cancer patients treated with radiotherapy from December 2017 to November 2018 at a single geographic site of an integrated health care system were evaluated. The first 20 patients were prior to treatment plan evaluation software implementation and the second 20 patients were after implementation. All patients had pathological early stage breast cancer status post breast conserving surgery. The RTOG and NRG Oncology guidelines for defining target volumes and critical structures provided standardization. All patients received 4256 cGy in 16 fractions to the entire breast only via tangent fields with field-in-field technique, with PTV_WB_EVA coverage goal of V95% >95-93%. Critical structures defined included body, contralateral breast, heart, left anterior descending (LAD) vessels, and ipsilateral and contralateral lungs. Dosimetric goals were unchanged before and after implementation. Certain dosimetric parameters (such as PTV_WB_EVA V95%, body V107%, and heart Dmean) were specifically tracked by the
Results

Twenty eight patients had left breast cancer. PTV_WB_EVA volume ranged from 237.4 to 1760.2 cc. Relevant dosimetric parameter changes after software implementation are shown in the table. Other dosimetric parameters assessed were minimally if at all changed after software implementation.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Prior to treatment plan evaluation software</th>
<th>After treatment plan evaluation software</th>
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</thead>
<tbody>
<tr>
<td>PTV_WB_EVA</td>
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<td></td>
</tr>
<tr>
<td>mean V95%</td>
<td>92.9%</td>
<td>94.3%</td>
</tr>
<tr>
<td>% meeting V95% criteria</td>
<td>50%</td>
<td>75%</td>
</tr>
<tr>
<td>mean D99%</td>
<td>2494 cGy</td>
<td>2860 cGy</td>
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<tr>
<td>Body</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean V107%</td>
<td>8.9 cc</td>
<td>3.6 cc</td>
</tr>
<tr>
<td>% meeting V107% criteria</td>
<td>70%</td>
<td>90%</td>
</tr>
<tr>
<td>Heart (left breast cancer only)</td>
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<td></td>
</tr>
<tr>
<td>mean Dmean</td>
<td>122 cGy</td>
<td>91 cGy</td>
</tr>
<tr>
<td>mean D5%</td>
<td>500 cGy</td>
<td>244 cGy</td>
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<tr>
<td>mean D0.03cc</td>
<td>1823 cGy</td>
<td>1462 cGy</td>
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<td>LAD vessels (left breast cancer only)</td>
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<tr>
<td>mean Dmean</td>
<td>535 cGy</td>
<td>427 cGy</td>
</tr>
</tbody>
</table>

Conclusions

Treatment plan evaluation software implementation incidentally improved whole breast radiotherapy plan quality. Most notable improvements were evident in PTV coverage as well as heart and LAD vessels avoidance. These improvements may be clinically relevant for certain patients.

References


Cancer (NSCLC) in a Military Community Setting

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Purpose

We compared our institutional outcomes for early stage non-small cell lung cancer treated with definitive SBRT to recently published prospective data in order to determine the generalizability to our military community setting. The United States military represents a unique patient population to study lung cancer outcomes due to universal access to care and routine follow-up.

Method

We retrospectively reviewed all patients who received definitive lung SBRT for both biopsy-proven and presumed NSCLC, from 2015-2019. All patients were staged with PET-CT and reviewed at our multidisciplinary thoracic tumor board prior to receiving SBRT. 87 patients were identified and 94 lesions were treated. 68 (72.3%) patients had biopsy proven NSCLC while 26 (27.6%) patients had presumed lung cancer determined by probabilistic modeling. 45 (66.2%) adenocarcinomas and 20 (29.4%) squamous cell carcinomas were identified. The median tumor size was 1.70 cm (range 0.60-5.50) in greatest dimension, and the median PTV volume was 21.95 cc (range 5.60-150.20). The majority of patients received 50 Gy in 5 fractions prescribed to the PTV. Established RTOG planning parameters and normal tissue constraints were utilized. The median follow-up time was 18.0 months.

Results

94 tumors (T1=70, T2=21, and T3=3); 53 (60.9%) male and 34 (39.1%) female; median age, 78 years [range, 56-90]. Median FEV1 and DLCO at enrollment were 80% (range, 26%-112%) and 57% (range, 23%-122%), respectively. At time of review, 2 patients had a primary tumor recurrence which presented as involved lobe failure. The primary tumor control and involved lobar control rates at 18 months were both 97.8%, while 5/94 (5.5%) patients experienced regional failure. Combined, 7/94 (7.4%) patients developed local-regional failure, while 7/94 (7.4%) patients experienced disseminated failure. Disease-free and overall survival rates were 85.0% and 80.9% respectively, at a median follow-up of 18.0 months. Treatment-related grade 3 toxicity was noted in one patient (rib fracture). No grade 4 or 5 toxicities were documented.

Conclusions

We observed excellent outcomes and low Grade 3 or higher toxicities, consistent with recently published prospective data from the RTOG. The military’s unique health care system with universal access to care, access to PET staging and imaging surveillance, and routine follow-up may have contributed to our outcomes. Additionally, nearly 30% of our patients lacked biopsy confirmation highlighting one difference between community practice and clinical trials. This review compares favorably to the previously published prospective data, supporting excellent rates of local control and toxicity in the treatment of early stage NSCLC with SBRT.

References

STARS/ROSEL Combined Analysis
RTOG 0618
RTOG 0236

Categories

Clinical investigations

Purpose

It is difficult to keep up with the pace of information in cancer care. During the beginning of residency in 2016, real-time resources were scarce in Radiation Oncology. The development of free, online resources such as QuadShotNews, econtour.org, and Rad Onc Tables have recently emerged to provide dynamic tools to stay abreast of the latest developments in our field. We believe it is possible to maintain an actively updated collection of clinical trials through a participating audience to place evidence at the fingertips of busy practitioners.

Method

From 2016-2019, a process was developed to objectively present findings from clinical trials, while translating commentary and opinions from the thought leaders in our field. Resources such as ASCO and ASTRO guidelines, ASTRO Refresheres, RadOncQuestions.com, Essentials of Clinical Radiation Oncology, and the resources mentioned above were
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Compiled and linked appropriately. A consistent outline format was applied to all disease sites. Summary boxes were written to drive home clinical pearls. Read by QXMD was recently utilized as a critical resource for discovering landmark studies, with journals followed including Advances in Radiation Oncology, Brachytherapy, IJROBP, JAMA Oncology, JCO, Lancet Oncology, PRO, and Radiotherapy and Oncology. After the backbone of more than 500 pages of Google Documents had been compiled, RadOncReview.org was built the week of ASTRO 2019 to provide a landing page and mission statement. Business cards were then handed out, and a Twitter account (@radoncreview) was launched for marketing. Collaboration was encouraged by allowing all anonymous to suggest changes on all documents without requiring a login. Google Analytics was utilized to provide data for visitors to RadOncReview.org, which was supplemented by a manual review of commentary on Google Documents to gauge audience participation.

Results

Since launching RadOncReview.org on 9/15/2019 (Tuesday of ASTRO), there have been 166 unique site visitors from the United States, 21 from Germany, two from Hong Kong, and one from Egypt, India, Japan, Sri Lanka, Philippines, Saudi Arabia, and Singapore. There has been an average of 42 individual site visitors per week users with peak site visitors during any week of 48 unique users on 9/22-28/2019 (one week post-ASTRO) followed by a twitter-influenced surge of 76 unique users the partial week of 10/20/2019 to 10/24/2019. Contributions, however, have been limited. Of 13 unique documents, only one user has suggested an edit, which involved headers under the Constraints and Toxicity section.

Conclusions

Capturing unique weekly users appears to be sustainable in the short term. However, a participating audience is difficult to enlist. We welcome input from ACRO and ARRO for improving this resource and make it available to all the residents as part of their educational resources.

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Categories

Physics/technology

70

Outcomes of Patients with Stage IIIC Endometrial Cancer Treated with Adjuvant Sequential Chemotherapy followed by Marrow-Sparing IMRT- A Single Institution Experience

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Purpose

Optimal adjuvant treatment of patients with stage IIIC endometrial cancer is not well established, with GOG 258 suggesting no statistically significant improvement in recurrence-free survival or overall survival for patients treated with adjuvant sequential chemoradiation therapy versus adjuvant chemotherapy alone, possibly secondary to increased risk of distant metastases with delay in systemic treatment despite improved locoregional control seen with additional of radiation therapy. Our approach has traditionally been adjuvant sequential chemotherapy consisting of 6 cycles of Carboplatin/Taxol, followed by pelvic +/- para-aortic external beam radiation therapy with vaginal cuff brachytherapy boost. We utilize marrow-sparing IMRT to reduce incidence of hematologic toxicities during radiation therapy, with goals of improving completion rate. We sought to evaluate whether this sequencing could result in improved locoregional control with preservation of benefit seen in distant control with chemotherapy.

Method

A retrospective analysis of 68 patients with FIGO stage IIIC endometrial cancer underwent surgical management between March 2008 and February 2018 was performed. Median age at diagnosis was 63 (range 35-83). 39 patients were FIGO Stage IIIC and 29 patients
were FIGO stage IIIC2. 38 patients had endometrioid histology, 5 patients had clear cell histology, 13 patients had serous histology, and 12 patients had mixed histology. Endpoints assessed were distant metastases, locoregional control, recurrence-free survival and overall survival, all defined as time from initial surgical management to death or recurrence.

Results

All patients received adjuvant chemotherapy followed by radiation therapy, with 63 patients receiving all 6 cycles of chemotherapy (range 3-6), with 100% completion rate of radiation therapy. All patients received external beam radiation therapy utilizing marrow-sparing IMRT to 45-50.4 Gy in 25-28 fractions to the pelvis (25%) versus pelvis & PA LNs (75%), followed by vaginal cuff brachytherapy boost. Median follow-up was 42 months (range 16-124 months). 20 of 68 patients (30%) developed recurrent disease, with 10 patients developing only distant metastases and 8 patients developing synchronous regional and distant metastases. Isolated locoregional recurrence occurred in 2 patients. Four-year Kaplan-Meier risk of isolated initial locoregional recurrence, isolated distant relapse, and synchronous local/distant relapse were 3.3%, 16.7%, and 10.9%, respectively. Four-year Kaplan-Meier relapse free survival and overall survival estimates were 71.8% and 81.0%, respectively.

Conclusions

Our single-institution data supports the use of adjuvant sequential chemotherapy followed by marrow-sparing IMRT for patients with stage IIIC endometrial cancer with high completion rate and favorable overall survival, locoregional control, and distant control when compared to historical data. Isolated locoregional recurrence was a rare occurrence, with the majority of patients who recurred developing either distant recurrence alone or synchronous distant and locoregional recurrence. Prospective evaluation of this sequencing of therapy is warranted.

Categories

Clinical investigations

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No Local Control Benefit with Implanted Fiducial Markers or Breath Hold Technique for Stereotactic Body Radiotherapy for Hepatocellular Carcinoma

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Purpose

Hepatocellular carcinoma (HCC) is a common malignancy worldwide with rising incidence and death rates. Stereotactic body radiotherapy (SBRT) is increasingly utilized for HCC as better imaging and motion management techniques allow for high doses with low rates of serious side effects. However, patient set-up and image verification remain a challenge. This study investigates clinical outcomes for SBRT used to treat HCC with respect to fiducial marker use and motion management technique.

Method

Patients with HCC treated with SBRT were retrospectively reviewed. Patients without post-treatment imaging were excluded. Fiducial marker use included implanted fiducial markers, radiopaque injected drug eluting beads or lipiodol, or other nearby radiopaque markers such as surgical clips or calcifications. Motion management techniques included either free-breathing (FB) utilizing 4D computed tomography or the use of inspiratory breath hold (BH) via active breathing control. Local control was defined at the treated site and determined by post-treatment imaging as read by institutional radiologists, multi-disciplinary discussion, or pathologic evaluation on transplantation. For the purposes of local control, patients were censored at the time of progression at the treated site or at transplant. Survival was defined at the time of patient death or at last follow-up.

Results

From January 2013 to June 2019, 48 consecutive patients with 53 lesions were treated with SBRT. Three patients were excluded for lack of post-treatment imaging, leaving 45 patients with 50 lesions for analysis. Median follow-up was 10.8 months (range 1.3 – 40.3 months). Median age was 68 (range 37 – 91) and 36 patients were male. 27 patients had stage T2 lesions and median tumor greatest dimension was 2.7 cm (range 1 – 10.2 cm). Median Childs Pugh score was 6 (range 5 – 10). Median BED10Gy dose delivered was 100 Gy (range 43.2 – 112.5 Gy). Fiducial markers were utilized in 23 patients (48%) and BH was utilized in 18 patients (37.5%). For the entire cohort, local control at 1 year and 2 years was 96.7% (95% CI: 78.6 – 99.5%) and 89.8% (95% CI: 62.3 – 97.9%), respectively, and overall survival at 1 year and 2 years was 72.7% (95% CI: 54.7 – 84.5%) and
57.8% (95% CI: 36.5 – 74.1%), respectively. There was no significant difference in local control with and without fiducial markers at 1 year (100% vs 94.7%) or 2 years (85.7% vs 94.7%) (p = 0.85). Similarly, there was no difference in 1-year local control with use of FB vs BH (100% vs 93.8%, p = 0.62). Grouping patients by these techniques (FB + fiducials, FB no fiducials, BH + fiducials, BH no fiducials) revealed no significant difference between these groups.

Conclusions
There is no local control benefit with implanted fiducial markers or use of breath hold technique making SBRT the only completely non-invasive treatment option for patients with HCC.

Categories
Clinical investigations
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High Rates of Pathologic Response after Stereotactic Body Radiotherapy for Hepatocellular Carcinoma
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Purpose
Hepatocellular carcinoma (HCC) is a common malignancy worldwide with poor outcomes. While surgical management has been the gold standard, patients are often unfit for surgical procedures, especially for liver transplantation. Increasingly other treatment options have been utilized to treat patients as a bridge to transplant, including stereotactic body radiotherapy (SBRT). SBRT has been described as effective and safe with high rates of pathologic response. This study reports pathologic response rates with SBRT for HCC at our institution.

Method
Patients with HCC treated with SBRT prior to liver transplant were retrospectively reviewed. Pathologic response was assessed based on institutional pathologist report. Complete response was defined as the presence of no viable tumor at the treated site. Partial response was defined as any viable tumor at the treatment site. Comparison with imaging response was performed with radiologic response determined as read by institutional radiologists or by multi-disciplinary discussion.

Results
From January 2013 to June 2019, 48 consecutive patients with HCC with 53 lesions were treated with SBRT. Seven of these patients subsequently had liver transplant. Five patients were male and the median age was 55 (range 51 – 69). Four patients had baseline Childs Pugh scores higher than B7 (three had B8, one had C10). The median time to transplant was 6.0 months (range 2.7 – 11.3 months). On evaluation of the explanted liver, 6 patients (85.7%) had a complete pathologic response and 1 had partial pathologic response (14.3%). One patient was noted to have two viable tumors outside of the treated volume. There were a median of 2 imaging examinations after SBRT but before transplant (range 1 – 3). In all patients, radiologic response correlated with pathologic response, except for the one patient with viable tumors at explant which were not described on imaging pre-transplant. At the time of last follow-up (median 12.1 months, range 7.2 – 36.0 months), all patients were alive.

Conclusions
For patients with HCC, SBRT is an effective bridge to transplant with excellent pathologic complete response rates, even in patients whom traditionally were not recommended for SBRT given more unfavorable baseline liver function.

Categories
Clinical investigations
79

Late Distant and Potential Local Failure of Hemangiopericytoma Treated with Surgical Resection and Adjuvant Radiation Therapy
Dr. David M Harris, Dr. John A Fiveash
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Purpose
Hemangiopericytomas are rare solitary fibrous tumors of the central nervous system. They have a tendency to metastasize outside of the CNS, with distant failures occurring potentially years after treatment. Research by Guthrie et al has shown the rates of 10 and 15 year metastasis of hemangiopericytoma to be 33 and 64% respectively. Treatment for hemangiopericytoma typically involves surgical resection followed by adjuvant radiation therapy (either with standard fractionation or stereotactic radiosurgery). Herein, we report a case
of late distant and possible local failure of hemangiopericytoma.

**Method**

A 47 year old female presented in 2008 with worsening headaches. MRI imaging revealed an intracranial tumor in the left parietal lobe. The tumor was monitored with MRI and found to have grown one year later. She underwent left craniotomy with surgical resection of the tumor with subsequent MRI showing no gross residual disease. Pathology revealed the tumor to be a WHO grade II hemangiopericytoma. She then received adjuvant hypofractionated stereotactic radiation therapy to 30 Gy in 5 fractions to the resection cavity.

**Results**

She tolerated the radiation treatment with minimal toxicity. She was followed with regular MRI imaging of the brain and CT imaging of the thorax, abdomen, and pelvis, on a yearly basis with no sign of recurrence for 9 years. In 2018 abdominal imaging revealed a new liver mass. The mass was resected and found to be a solitary fibrous tumor, pathologically identical to her original hemangiopericytoma upon review by neuropathologists. The case was discussed in tumor board and a decision was made to continue surveillance. Within 12 months, imaging identified an enlarging metastatic lesion at T3. This was treated with 30 Gy in 5 fractions stereotactic body radiation therapy. Imaging at the same time also revealed an enlarging retroperitoneal nodule and 2 right lung nodules. Genetics report showed that tumor cells were positive for BCL-2, STAT6, and CD-34. She was started on pazopanib for systemic therapy. At last follow up MRI of the brain showed enhancement in the left parietal resection cavity, indicating possible local failure.

**Conclusions**

Hemangiopericytoma is a rare solitary fibrous tumor that has propensity to local and distant failures many years after treatment. Adjuvant systemic therapy after surgery is not currently standard of care. There is a need for improved risk stratification of these tumors to identify appropriate candidates for adjuvant or maintenance systemic therapy and/or dose escalation of radiotherapy to decrease recurrences.

**References**


**Categories**

Clinical investigations

80

**Local Therapy Influences Patterns of Disease**

**Progression in Stage IV Synchronous Oligometastatic Breast Cancer**

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**Purpose**

While evidence is emerging in favor of local therapy for patients with oligometastatic disease, very few studies have assessed the role of aggressive local metastases directed therapy in breast cancer-related disease.

In our study, we aim to assess the patterns of failure following standard systemic therapy with or without the addition of metastasis directed local therapy (MDT) in stage IV breast cancer patients with 1 to 5 metastatic lesions.

**Method**

Stage IV breast cancer patients at diagnosis with 1-5 metastases were included. At first progression, failures were categorized into two different groups: failures at any index sites (breast or regional nodes or metastatic site/s at diagnosis) and non-index sites. Clinical and treatment related factors were compared for both groups using chi-square test. Cox’s model was used to estimate the risk of progression.

**Results**

Fifty-one patients treated from 2002 to 2018 were included. Median follow-up was 40 months (range 10-60 months). Most patients (47%) had 2-3 metastatic lesions, and 70.5% had hormone receptor positivity at diagnosis. 62.7% received primary treatment to breast before first progression and 17.6% received MDT to all metastatic sites. Of the 43 patients (84.3%) that progressed, 34.8% events occurred at index sites while the remaining 65.2% progressed at non-index sites. Definitive treatment to primary breast lesion was associated with delayed progression at
Analysis of the Frequency, Methodology and Delivery of Consensus Recommendations

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Purpose

Contouring is a critical element of radiation treatment planning to ensure both adequate dose to disease and sparing of nearby normal organs-at-risk (OARs). Research has demonstrated that contouring is highly variable between providers, and that variations in contouring can result in detrimental patient outcomes, including decreased survival. As a result, formal guidelines have been published in an effort to help standardize the contouring process. We sought to assess trends in the publications of these guidelines as well as the methodologies used to both generate and deliver consensus recommendations.

Method

A comprehensive search was conducted in PubMed, Embase, Cochrane, Web of Science and Scopus databases using controlled vocabulary and keywords related to contouring guidelines published between 1995 and 2019. This resulted in 11,124 unique citations. These abstracts were screened for relevance, which identified 332 potentially relevant publications. The full text of these articles was reviewed for final inclusion by two reviewers, with any disagreements resolved by a third reviewer. Inclusion criteria included studies that were in English, and had specific recommendations regarding contour delineation (rather than recommendations for dosing or other aspects of treatment planning). Of the 332 potentially relevant publications, 143 met the inclusion criteria.

Results

There was an increase in the publication of consensus recommendations over time, with 0 articles published from 1995-99, 10 published from 2000-2004, 22 published from 2005-09, 45 published from 2010-14 and 66 published from 2015-19. A large majority (97%) were publicly accessible. The most common disease sites were head and neck (23%), gastrointestinal (13%), and gynecologic (12%). Of guidelines focusing on a particular treatment technique, conventional external beam treatment was the most common (80%), with others focused on brachytherapy (13%), SRS/SBRT (6%), or protons (1%). 64% of guidelines were formally endorsed by a national or international organization. When specified, the mean number of participants on the consensus committee was 14 (IQR 7-16), with 37% of panels including a radiologist. A minority of publications (15%) included statistical analyses of variation amongst expert contours. 82% of publications included representative axial imaging, with a mean number of images of 21 (IQR 8-30). 13% also published a full image or contour set highlighting the recommendations.

Conclusions

This review highlights trends in consensus contouring publications, including an increase in such
publications over time. Guidelines are often backed by national or international groups and are most commonly focused on disease sites regarded as difficult to contour, such as head and neck. Most include at least some representative imaging, though publication of complete reference imaging data-sets is lacking. There is also an opportunity for more formal analysis of expert contours to help generate consensus recommendations.

Categories
Socioeconomic/ethical issues/health outcomes research

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Gonadal-Sparing Total Body Irradiation with the Use of Helical Tomotherapy for Nonmalignant Indications

Austin J. Sim1, Khaled Dibs2, Jose A. Penagaricano3, Kujtim Latifi3, Genevieve A. Garcia1, Michael L. Niedler1, Sungjune Kim1, Timothy J. Robinson3

1H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA. 2King Hussein Cancer Center, Amman, Amman, Jordan

Purpose
To report the feasibility and methodology of gonadal-sparing total body irradiation (TBI) with the use of helical tomotherapy (HT) as a part of a conditioning regimen prior to bone marrow transplant (BMT) for nonmalignant indications.

Method
A 20-year-old African American male with severe sickle beta-zero thalassemia underwent a matched (sibling) allogeneic BMT with a conditioning regimen of alemtuzumab and TBI, planned and delivered with helical tomotherapy. Defined organs at risk were the lungs and brain (contracted by 1 cm each) and the testicles (expanded by 5 cm). The planning target volume (PTV) was defined as the entire body minus the contracted lung/brain and expanded testicles. Prescription was set such that 96% of the PTV received 3 Gy in a single fraction. In-vivo dosimetry of the testicular dose was performed using nanoDot™.

Results
The primary dose objective to the PTV was achieved with a conformity index of 0.96 and a homogeneity index of 1.35. The beam-on time was 43 minutes. Maximum and the median dose to the testes were 0.53 Gy (18% of the prescribed dose) and 0.35 Gy, respectively. The in-vivo dosimetry showed the testes to receive 0.48 Gy. Mean doses to the brain, lungs, heart, right kidney, and left kidney were 2.83 Gy, 3.06 Gy, 2.80 Gy, 3.27 Gy, and 3.22 Gy, respectively. In-vivo dosimetry demonstrated differences between the planned and delivered dose between -17.8% to 14.6%.

The patient successfully underwent bone marrow transplant after successful completion of the conditioning regimen. He was discharged after an uneventful hospital course and was continued on sirolimus. Laboratory studies on follow-up demonstrated successful engraftment and mild, transient transaminitis, attributed to graft versus host disease. The latter was controlled with minor sirolimus dose adjustments. His most recent follow-up was 25 months status post transplant and unremarkable.

Conclusions
As illustrated by this case, HT is able to achieve testicular dose sparing to preserve fertility when used for TBI as part of the conditioning regimen for patients with non-malignant diseases prior to stem cell transplant. This is achievable with the added benefits of improved dose homogeneity and image guidance.

References


Categories
Physics/technology

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Scar bolus omission during adjuvant intensity modulated radiotherapy (IMRT) does not
increase risk of incisional recurrence for oral cavity cancers

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Purpose

Locoregionally advanced oral cavity cancers have an increased risk of locoregional recurrence despite multimodality therapy. In an effort to decrease scar recurrences in the postoperative setting, bolus has historically been used to increase the dose to the neck scar in intermediate and high-risk contexts. Since transitioning to IMRT for most post-operative oral cavity cases, we have routinely omitted bolus placement on the neck scar. Here we examine rates of scar recurrences using this approach.

Method

This is an IRB approved retrospective study. Patients with intermediate or high risk squamous cell carcinoma of the oral cavity treated with post-operative IMRT were identified from an institutional database. Patients were treated using tomotherapy based IMRT (Accuray, Sunnyvale CA). Demographics, clinical/pathologic parameters, dosimetric data, and cancer-related outcomes were recorded and analyzed. SPSS v 22 (IBM, Montauk, NY) was used to determine Kaplan Meier estimates for disease control and survival.

Results

28 pts met inclusion criteria for this analysis and were treated from 2009 to 2017. Median age was 56 years old (range 35-75); 59% were male. All patients underwent complete resection of the primary tumor with selective neck dissection. Subsites included 11 floor of mouth (40%), 6 oral tongue (21%), 5 buccal mucosa (18%), 3 lower lip (11%), 2 hard palate (7%), and 1 retromolar trigone (4%). 71% were pathologically node positive; 36% had extracapsular extension (ECE). Concurrent chemotherapy was used in 53% of patients. 24 patients (86%) were treated using SIB technique. The postoperative neck was irradiated in all cases. Median dose to the highest risk volume was 6000 cGy (range 5800-6600 cGy). Median treatment package time was 95 days (range 76-137 days). Median follow up for surviving patients after treatment was 40 months (range 1-111 months). Three patient experienced a local recurrence (range 4-54 months). Five patients developed distant metastatic progression at a median of 4 months (range 1-54 months). One patient experienced a suspected local and regional nodal relapse and there have been no scar recurrences. 3-year actuarial estimates for DFS and OS are 64.3% and 82.1%%.

Conclusions

Scar recurrences after post-operative IMRT are rare. Bolus omission has not compromised disease control along the scar.

Categories

Clinical investigations

Dosimetric Comparison of Cone and Multileaf Collimator based Linear Accelerator

Radiosurgery for Arteriovenous Malformations

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Purpose

Stereotactic radiosurgery (SRS) is an established treatment for arteriovenous malformations (AVMs), with both gamma knife and linear accelerator (LINAC) modalities used. Recent studies suggest that LINAC and gamma knife have similar outcomes in terms of AVM obliteration and toxicity,1 that the volume of normal tissue exposed to 12Gy (V12) is associated with radionecrosis,2 and that the volume of normal tissue exposed to 4Gy (V4) predicts neurocognitive decline and secondary malignancy.3 Our study aims to determine whether cone or MLC treatment delivery offers better dosimetry, which would predict differences in obliteration and toxicity between the two modalities. We hypothesize that for low volume AVMs (gross target volume <2cc), cones will have better conformity as measured by the ratio of the 50% prescription isodose line to the prescribed treatment volume (R50), and a more favorable V4 and V12 compared to MLCs.

Method

A retrospective cohort study was conducted on 26 patients treated for AVMs with gross target volume <2cc using LINAC based SRS between the
years 2003 to 2017. Demographic data was collected through review of each patient’s electronic health record. Dosimetry measurements were calculated from each patient’s treatment plan.

Shapiro-Wilk tests were used to evaluate normality. A two-sample t test was used to compare V4 and V12 between cones and MLCs. A Wilcoxon Rank Sum test was used to compare R50. A probability value of <0.05 was defined as statistically significant.

Results

For cone based treatment, the mean V4 was 13.903cc, the mean V12 was 2.1107cc, and the mean R50 was 3.42. For MLC based treatment, the mean V4 was 24.1976cc, the mean V12 was 3.6001cc, and the mean R50 was 3.61. Cones had significantly lower V4 (p=0.0152) and V12 (p=0.0114) compared to MLCs. No significant differences in R50 were found.

Conclusions

Cone treatment delivery appears to have favorable dosimetry with regard to V4 and V12 when compared to MLC treatment delivery. This predicts fewer long term complications, which is particularly important because the population treated for AVMs is relatively young. There was no significant difference in conformity as measured by R50%.

We plan to evaluate rates of radionecrosis and neurocognitive adverse effects in cone and MLC treatment delivery, as well as differences in rate of obliteration and time to obliteration between the two modalities.

References
The majority of patients presented after BCR following RP (N=28), definitive RT (N=27) or RP+post-op RT (N=6). Prior to USPIO-MRI, 20/69 patients had cN1 disease based on abdominal-pelvic CT/MRI, Bone Scan, Prostascint-scan, and F18 Choline, Axumin or PSMA PET/CT. The mean(median) USPIO(+) LNs was 5.2(3) Range=[1-32]. Patients had (+) pelvic (95%, mean n=2.5), paraaortic (43%, mean n=2.3), and/or perirectal LNs (19%). Notably, 51% of patients with (+) pelvic nodes had at least one involved common iliac node.

At median follow up of 29.5(44.6) Range=[5-127] months, PCS and OS were 58/69 (84%) and 11/11 patients died of PC. At last follow up, 40 patients remained BCR-free and the median time to BCR (N=29) was 25.9 months after USPIO-guided RT. For patients with follow-up imaging, recurrences predominantly occurred out-of-field (superior to the elective LN fields or in osseous sites). No patients experienced >CTCAE grade 2 AEs.

Conclusions

In this cohort of 69 patients with predominantly recurrent PC, USPIO-directed RT appears to be well-tolerated, feasible and resulted in very encouraging biochemical control rates. Elective RT to common iliac nodes may be beneficial in patients with recurrent pelvic nodal disease.

Categories

Clinical investigations

A 9-year review of interstitial HDR brachytherapy for soft-tissue sarcoma: A single institution experience and review of literature.

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Purpose

The purpose of this project is to detail a single institution’s experience with interstitial HDR brachytherapy for soft-tissue sarcomas. This review investigated the treatment paradigms of soft-tissue sarcomas at our institution with special attention to acute and long-term toxicities.

Method

We conducted a retrospective review of the patients with a diagnosis of a soft-tissue sarcoma who underwent interstitial HDR brachytherapy at our institution. Study results are summarized using descriptive statistics.

Results

Between September 2010 and September 2019, 18 patients with a soft-tissue sarcoma diagnosis were treated with temporary interstitial HDR brachytherapy with iridium-192 at our center. Two of the patients received brachytherapy twice for a total of 20 brachytherapy procedures. Median age at diagnosis was 55.5 years old (range 29-88). The 3 most common histologic subtypes were undifferentiated pleomorphic sarcoma (n=5), spindle cell sarcoma (n=3), and myxofibrosarcoma (n=3). Eleven patients had sarcoma of the lower extremity, with the next most common location being trunk (n=4). The most common dose fractionations were 12 Gy in 3 fractions (n=7) and 16 Gy in 4 fractions (n=7). Of the 18 patients, 2 (11%) underwent a 2nd brachytherapy procedure for recurrence following surgical excision with negative margins. Both recurrent cases received a dose of 32 Gy in 8 fractions. The interval from prior brachytherapy was 14 and 20 months. Four patients (22%) underwent their first brachytherapy treatment for a local recurrence. Of the 14 patients treated with upfront with brachytherapy (ie, not for local recurrence), 12 patients had pre-operative external beam radiation therapy (EBRT) followed by surgery with planned positive margins and catheters placed at the time of surgery. The pre-operative external beam radiation treatment was 50Gy in 25 fractions for 10 (55%) of those patients. The median number of catheters used for all 20 procedures was 13 (range 5-24). The median interval between catheter placement and the first HDR treatment was 7 days. Seven patients had acute side effects including cellulitis (4), seroma formation (1), edema (1), and a necrotizing skin infection (1). Six patients had a long-term toxicity which included lymphedema (1), skin fibrosis/joint stiffness (3), lymphedema (1), and a non-healing wound (1). Of the 14 patients treated with brachytherapy as a part of their initial treatment, 5 (35%) developed a local recurrence. The average time from brachytherapy procedure to local recurrence was 13.2 months (range 2-49). Seventeen patients had reliable follow-up data which showed that 10 (59%) developed distant metastases. Six patients (33%) had both local recurrence and distant metastases.

Conclusions

Interstitial HDR brachytherapy boost for soft-tissue sarcomas in the setting of a positive surgical margins is a safe and feasible treatment modality.

Categories

Clinical investigations
Increase in Post-Chemoradiation Percent Frequency of Peripheral Blood Myeloid-Derived Suppressor Cells in Patients with Glioblastoma with Progressive Disease

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Purpose

Myeloid-derived suppressor cells (MDSC) have been reported to have prognostic importance in patients with glioblastoma. Few studies have investigated this cell type in fresh, non-frozen peripheral blood samples in patients with this primary brain tumor type. Additionally, there is a limited understanding of the effect of chemoradiation (temozolomide/radiation therapy-60 Gy in 30 fractions) on MDSC percent frequency (%fx) of peripheral blood mononuclear cells. This study aims to contribute to the limited information regarding peripheral blood MDSC in patients with glioblastoma after standard adjuvant chemoradiation.

Method

Fresh, peripheral blood samples were collected from patients at a single institution with a new diagnosis of glioblastoma who underwent surgical resection followed by adjuvant chemoradiation. Peripheral blood mononuclear cells (PBMC) were isolated from whole blood through density gradient centrifugation. PBMC were incubated with mouse anti-human monoclonal antibodies against CD33 and HLA-DR. Dead cells were identified for exclusion using a viability dye. Multi-parametric flow cytometry was performed on fixed PBMC using a BD FACSCelesta. Data were analyzed with FlowJo v10 with the following gating strategy: non-debris, singlet, alive cells, events with forward and side scatter properties consistent with peripheral myeloid cells, CD33+HLA-DR+. MDSC %fx was compared at pre-adjuvant baseline to post-adjuvant chemoradiation which was defined as between four to nine weeks after completion of chemoradiation. Progression was identified by serial MRI brain imaging and defined as progression on imaging or death. The difference in %fx in progressors and non-progressors was evaluated via a two-tailed, unpaired t-test with GraphPad (Prism).

Results

Blood samples from nine patients (two women/seven men) were analyzed. Six of nine progressed within one year of diagnosis with one patient death. Two of three non-progressors and none of the progressors were identified to have tumor tissue with methylation of the MGMT gene. No IDH mutations were identified within tumor tissue samples from the cohort. The median MDSC %fx at the post-surgical, pre-chemoradiation baseline was 27.5% (range: 27.3 to 56.6%) for non-progressors and 22.5% (range: -13.0 to 48.6%) in progressors. The difference in %fx of MDSC post-adjuvant chemoradiation, compared to baseline, for non-progressors was -19.4% (range: -5.6 to -26.1%) and +8.1% (range: -17.7 to 13.2%) in progressors (p=0.04).

Conclusions

In this cohort of patients with new diagnosis of glioblastoma, the %fx of MDSC increased following adjuvant chemoradiation in patients that progressed within the first year of diagnosis. Additional studies are needed to understand the effect of adjuvant therapy on MDSC %fx and the relationship of this cell population and tumor control.

Categories

Translational science

The U.S. Online News Coverage of Proton Beam Radiation Therapy Based on a Google News Search

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Purpose

Proton beam therapy (PBT) has dosimetric advantages over photon radiotherapy, but randomized data supporting its utility remain scarce. These controversial issues have raised considerable attention from many news sources at the local and national level, which has the potential to impact patients’ and physicians’ views
of PBT as well as patients’ likelihood to seek out PBT centers. The purpose of this study was to characterize online news coverage relating to PBT.

Method

Google News, a searchable news aggregator of thousands of news websites, was queried in July 2019 to search U.S. news sites over a 9-year period (2010-2018) based on the search terms “proton therapy”, “proton radiation”, or “proton beam therapy”. Up to the top 100 search results were recorded based on Google News’ algorithm, sorting results by relevancy and popularity in real-time. When articles did not meet these criteria or were unavailable from nonworking URLs or from links requiring subscriptions, the next article identified by the search was selected. Two reviewers evaluated the articles in consensus. The following information was recorded for each article: article source, predominant theme, whether the article included a patient story, whether the article mentioned a specific facility offering PBT, whether the article mentioned a radiation oncologist or radiation oncology, and whether the article was directly consulting or quoting a radiation oncologist. In addition, the article’s overall stance toward PBT was characterized as leaning favorable, unfavorable, or neutral. Data were summarized with total counts and percentages calculated.

Results

In the 259 total online news articles that were analyzed between 2010-2018, the distribution of news sources was as follows: 34% regional news outlet, 24% national news outlet, 11% entertainment or culture news outlet, 17% business news outlet, and 14% radiation oncology news outlet. Only two online articles were from peer-reviewed journals. The most common themes were the financial concerns of proton therapy (24%), opening of new proton therapy centers (19%), benefits of proton therapy (14%), and advances in proton therapy technology (13%). About half (49%) of articles had a positive stance while 18% and 33% of articles were negative or neutral, respectively. National news outlets were balanced among positive, neutral, and negative stances, while regional outlets skewed positive. Almost a quarter of articles included a patient story, while over half of articles directly quoted a radiation oncologist.

Conclusions

A wide range of online news sources have addressed several issues related to PBT. Most articles had a positive stance toward PBT with regional news outlets more likely to report a favorable stance toward PBT compared to national news outlets. The financial toxicity of PBT was the most common theme. Since online news may impact public perception of PBT, radiation oncologists should be aware of the online coverage of PBT.

Categories

Socioeconomic/ethical issues/health outcomes research

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A Core Competency-Based Preclinical Curriculum Introducing Radiation Oncology to Medical Students

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Purpose

Radiation oncology is a multifaceted specialty which requires special attention to many core competencies in medicine - from ethical to professional to knowledge-based. We worked in conjunction with our medical school to design a two week course aimed to give medical students an introduction to the field of radiation oncology, regardless of intent to ultimately pursue the field.

Method

Baylor College of Medicine Curriculum Development Committee was contacted to co-design a core competency (CC) based curriculum for second and third year medical students. CC required for graduation were mapped; a structured proposal was submitted to the College and approved.

Results

The final curriculum included three CC themes required for graduation which were addressed during a two week course in radiation oncology for medical students prior to elective rotations: (1) Ethical challenges related to cancer and end-of-life care. (2) Identifying the role of radiotherapy in medicine. (3) Gathering anatomical information. Three structured modules with a case-study approach were utilized for learning. Self-assessments were required after each module. Student feedback is gathered after each rotation.

Conclusions

To address issues with diversity and inclusion in radiation oncology, a preclinical core competency based curriculum can introduce medical
students to the field at an early point in their career.

Categories

Socioeconomic/ethical issues/health outcomes research

Radiation Therapy Treatment of Squamous Cell Carcinoma of the Soft Palate

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Purpose

The National Cancer Institute’s SEER database estimates that there were 8,025 new cases of oropharynx cancer in the United States in 2015. It has been estimated at our institution that, of those, approximately 1 in every 4 has a primary soft palate tumor. Treatment options for soft palate squamous cell carcinoma (SCC) include surgery or radiotherapy alone, or surgery followed by postoperative radiotherapy. Platinum-based chemotherapy is often used concurrently with radiation in locally advanced disease. Here we describe our single-institution experience in treating soft palate SCC.

Method

A total of 159 patients treated with curative intent at our institution between 1963 and 2016 were retrospectively reviewed. Radiation treatment modalities included conventional external-beam radiotherapy, intensity-modulated radiotherapy (IMRT), intraoral cone, and low-dose rate interstitial implants in a few patients. We excluded with distant metastatic disease or histologies other than SCC as well as those who had received prior head and neck radiotherapy. Disease in all patients was retrospectively staged according to AJCC 7th edition staging guidelines.

Results

The median follow-up was 4 years, and 10.2 years for all living patients. Local control rates at 5 years were: T1, 87%; T2, 89%; T3, 66%; T4, 55%, and were essentially unchanged at 10 years after treatment. The 5-year cause-specific survival (CSS) rate was nearly identical for stage I-III patients (84%, 83%, and 85%) compared to stage IV (53%). Additionally, 5-year overall survival was similar between stage I-III patients (50%, 57%, and 54%, respectively), and approximately double that of stage IV patients (26%). A total of 13 patients had severe complications related to radiation treatment during or shortly after treatment, including one which was fatal. Severe complications included permanent PEG placement, osteoradionecrosis, and severe infection. Prior to treatment delivery, 11% of patients were found to have concurrent second head and neck primary tumors at a different subsite.

Conclusions

To our knowledge, this data set represents the largest and longest single-institution review of radiotherapy for this disease subsite. Excellent rates of local control can be achieved in T1-T2 patients. Additionally, 5-year CSS was equivalent between stage I-III patients. Severe complications with radiotherapy were similar to previously published oropharynx outcomes. IMRT has largely replaced conventional techniques, such as parallel opposed-field external-beam radiotherapy. Interestingly, the rate of synchronous second head and neck primaries was 11.3% in our study population. A recent large retrospective review by Bugter et al (Head and Neck, 2019) demonstrated a synchronous second head and neck primary rate of approximately 2%. This may suggest that the soft palate subsite is at a particularly high risk for synchronous second primary.

Categories

Clinical investigations

Comparing National Practice versus Standard Guidelines for the use of Adjuvant Radiotherapy and Chemotherapy Following Robotic Surgery for Oropharyngeal Squamous Cell Carcinoma

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Purpose
Evidence-based guidelines recommend adjuvant radiotherapy (RT) with or without chemotherapy when there are specific pathologic findings following transoral surgery for oropharynx cancer. We report the frequency with which patients in the National Cancer Database with standard indications for adjuvant therapy actually received such therapy.

**Method**

Using the National Cancer Database, a nationwide hospital-based registry run jointly by the American Cancer Society and Commission on Cancer we identified 2,514 patients with AJCC 7th edition cT1-3 cN0-2 cM0 squamous cell carcinoma of the oropharynx treated with robotic surgery. We considered five factors as indications for RT: positive margin, extranodal extension (ENE), pN2-3, pT3-4, or lymphovascular space invasion (LVSI). Positive margin and ENE were considered indications for chemotherapy. Data are presented as numbers and percentages of patients who are not coded as having receiving adjuvant therapies. Multivariate Cox proportional hazards analyses were used to compare overall survival (OS) between groups.

**Results**

A total of 2431 patients meeting inclusion criteria were identified. Of those, 75.8% (n = 1905) had at least one indication for adjuvant RT. Table 1 shows the number and percent of patients who did not receive adjuvant therapy based on specific and number of indications. Overall, 20.6% of patients with any indication for RT did not receive adjuvant RT. This included the 21.8% of patients with a positive margin (micro- or macroscopic) who did not receive adjuvant RT. Of the 943 patients with an indication for adjuvant chemotherapy, 35.2% of patients did not receive it. On multivariate analysis including 1013 patients with an indication for adjuvant RT, documentation for all risk factors, and known HPV status, the receipt of RT was associated with an improvement in OS (hazard ratio [HR] = 0.55, 95% confidence interval [CI] = 0.34–0.90, p = 0.02). On a similar analysis including the 491 patients with an indication for adjuvant chemotherapy, documentation for all risk factors, and known HPV status, the receipt of adjuvant chemotherapy was associated with improved OS (HR = 0.46, 95% CI = 0.26–0.82, p = 0.01).

**Table 1. Frequency of Adjuvant Radiotherapy following Robotic Surgery**

<table>
<thead>
<tr>
<th>Indication for Adjuvant RT</th>
<th>Total Number</th>
<th>Number Receiving RT</th>
<th>Percentage Not Receiving RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT3-4 disease</td>
<td>205</td>
<td>143</td>
<td>30.2%</td>
</tr>
<tr>
<td>pN2-3 disease</td>
<td>1586</td>
<td>1312</td>
<td>17.3%</td>
</tr>
<tr>
<td>LVSI present</td>
<td>557</td>
<td>471</td>
<td>15.4%</td>
</tr>
<tr>
<td>Positive margin</td>
<td>354</td>
<td>227</td>
<td>21.8%</td>
</tr>
<tr>
<td>Extranodal extension</td>
<td>729</td>
<td>625</td>
<td>14.3%</td>
</tr>
</tbody>
</table>

**Conclusions**

Analysis of a large national database suggests that most patients receiving robotic surgery for oropharyngeal cancer have at least one indication for adjuvant therapy; however, a large percentage of patients with indications for adjuvant therapy do not receive it, which may have a negative impact on overall survival in these patients.

**Impact of Radiotherapy Delay on Survival in WHO Grade III Gliomas: An Analysis of the National Cancer Database**

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**Purpose**

Anaplastic astrocytomas and oligodendrogliomas are primary brain tumors classified as World Health Organization (WHO) grade III. Standard of care treatment for these tumors includes surgical resection followed by adjuvant radiotherapy (RT) and chemotherapy; however, the optimal time interval between surgery and RT remains unclear. Therefore, this study aims to use a large cohort from the National Cancer Database (NCDB) to identify predictors for and clinical impact of time from surgical resection to initiation of RT in these patients.

**Method**

The National Cancer Database (NCDB) was queried for patients with WHO grade III gliomas diagnosed from 2004-2015. The time interval between surgery and the start of RT was grouped into 1-30 days, 31-60 days, 61-90 days and >90 days. Overall survival (OS) was estimated via Kaplan-Meier and log rank tests. Univariate (UVA) and multivariable Cox regression (MVA) modelling was used to determine predictors of OS.

**Results**

A total of 8,886 patients (median age: 48 years) were included with a median time interval from surgery to RT of 35 days (Range: 1-706 days) and median OS of 51.3 months (Range: 0.85-155.6). On UVA, age ≤50, female gender, Hispanic or other ethnicity (not Caucasian or African American), KPS>60, achieving a gross total resection (GTR), unifocal disease, smaller tumor size, intensity-modulated RT (IMRT) and stereotactic radiosurgery, >15 RT fractions, low Ki-67, 1p19q co-deletion status, adjuvant chemotherapy, methylated gene status, and delaying RT 30-90 days predicted for improved survival. On MVA, initiation of RT 30-90 days following resection*, age <50*, unifocal disease*, smaller tumor size*, and treatment with chemotherapy (p=0.003) predicted for improved overall survival. For patients initiating RT 1-30 days following resection, the 1-, 5-, and 10-year OS rates were 76%, 38%, and 27%. For patients starting RT 31-60 days following resection, the 1-, 5-, and 10-year OS rates were 87%, 52%, and 37%, respectively and for the patients beginning RT 61-90 days following resection, the 1-, 5-, and 10-year OS rates were 89%, 57%, and 41%, respectively.

\* = p-value <.001

**Conclusions**

This analysis of the NCDB suggests that surgery to radiation timing is an important and actionable prognostic variable in the treatment of grade III gliomas. Our data indicates that receiving radiation between 1 and 3 months after surgical resection is associated with improved overall survival. Further studies are needed to evaluate the role of evolving molecular markers and the correlation of other modifiable treatment variables associated with this disease.

**References**


**Categories**

Clinical investigations

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**Oncologic Outcomes of Patients with Metastatic Melanoma status post Stereotactic Radiosurgery and Immunotherapy**

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**Purpose**

Use of immunotherapy in metastatic melanoma patients is a novel treatment modality, however the impact of combining gamma knife stereotactic radiosurgery (GK-SRS) and immunotherapy on in-brain progression free survival (PFS) and overall survival (OS) is still unclear.

Hence, we conducted a match-pair analysis on patients who underwent GK-SRS from the time that immunotherapy became approved.

**Method**

This is a single institution retrospective study of 172 patients with intracranial metastatic melanoma, who underwent GK-SRS from October 1991 thru December 2018. Of these, 43 patients with 120 lesions were treated during the era of immunotherapy, from January 2009 through December 2018.
All pts underwent frame based GK-SRS prescribed to the 50% isodose line, 23% underwent resection prior to GK-SRS and 11% received WBRT. The median prescribed dose was 24 Gy (10-24) and median tumor volume 3.27cc (0.02-56.7). All patients had an ECOG performance status ≤2. The cohort consisted of 98% Caucasians and 56% were male. Forty seven percent received immunotherapy (checkpoint inhibitor (PD1, BRAF, & MEK) inhibitor, or CTLA-4), 53% were either treated with another type of systemic treatment (Taxanes, platinum) or received no systemic treatment. Intracranial metastases were 23%, 21%, 12.5%, and 12.5% in right frontal, right parietal, left frontal, and left parietal lobes, respectively.

Results

With a median for up of 9 months, 62% of patients experienced in-brain tumor control whereas 38% were found to have in-brain tumor progression, most being regional rather than local failure. In the immunotherapy group, 75% had regional/in-brain tumor control while 46% of patients who did not receive immunotherapy had regional/in-brain control (p < 0.08). Median in-brain progression free survival (PFS) for those receiving immunotherapy was 19 months compared to 9 months in those who did not receive immunotherapy (p < 0.122). The overall survival (OS) for the whole cohort was 54%. Specifically, 43% of patients who received immunotherapy were alive vs. 64% of patients who did not receive immunotherapy (P < 0.17). On Kaplan Meier survival analysis, the median survival for patients who received immunotherapy was 9 months compared to 23 months in patients who did not receive immunotherapy (p < 0.4).

Conclusions

Our data suggest that despite the improvement in-brain (PFS) and loco-regional control when GK-SRS combined with immunotherapy there was no improvement in OS. Hence, this combination may have detrimental effects on clinical outcomes rather than inducing an abscopal / radoscopal effect systemically. Larger studies are warranted to confirm or refute this unexpected observation.

References


Categories

Clinical investigations

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Quality of Regional Nodal
Irradiation Plans in Breast
Cancer Patients – Can We
Translate Results from
Randomized Trials into the
Clinic?

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Purpose

Regional nodal irradiation (RNI) has been shown to improve disease-free survival (DFS) by 3-5% for breast cancer in 2 large randomized trials, which has led to wider adoption of this technique. Since the improvement in outcome is small, it is important that contouring and dose delivery are done appropriately, in order to realize this small advantage. The goal of this project was to audit our network program to determine the compliance of regional nodal coverage, contouring, and dosimetric parameters with respect to accepted guidelines.

Method

In our network, we have established a Clinical Pathway which guides indications for RNI for node-positive breast cancer patients. It also provides dosimetric parameters for patients who receive RNI. A retrospective review was performed on 183 patients found to have nodal macrometastases after upfront surgery, or involved nodes of any size after neoadjuvant chemotherapy. Radiation treatment plans were examined to determine what lymph node volumes were treated, whether treated nodes were contoured, quality of the nodal contouring, and whether target coverage and normal organ dosimetric constraints were met when RNI was delivered. Criteria for acceptable target coverage was defined as per the ongoing Alliance A011202 trial. Contours were reviewed by an expert breast radiation oncologist to determine whether they were acceptable or not based on the RTOG contouring atlas.
Results

Despite the presence of macrometastases on sentinel lymph node biopsy, lymph nodes were not treated at all in 2.2% (4/183) of patients. Of the remaining 179 patients who received some form of nodal irradiation, 18 patients received radiation to axillary levels 1 and 2 only, while 161 patients received RNI. The regional nodes were not treated when required in 7.3% (13/179) of patients. Of the 179 patients who received nodal irradiation, treated nodes were not contoured for 2.2% (4/179), and at least one region of lymph node contours was unacceptable in 16% (28/175). D90 for axillary level 3 was <90% in 7.5% (12/161) of patients, D90 for supravacular nodes was <90% in 11.2% (18/161), and D90 for internal mammary nodes was <80% in 3.7% (6/161). Overall, 14.9% (24/161) did not have adequate nodal target volume coverage. Mean heart dose was >4 Gy for 3.11% (5/161), and lung V20Gy was >35% for 8.70% (14/161).

Conclusions

Based on an audit of radiation plans across our network for node-positive breast cancer patients, there was good adherence to indications for regional nodal treatment. However, nodes were either not contoured or had unacceptable contour quality in about 18% of patients, and coverage did not meet acceptable criteria in 14.9%. Because the small DFS advantage seen in trials may be decreased with these deviations, routine clinical practice requires detailed peer review to fully translate results of clinical trials.

Categories

Clinical investigations

Safety and Efficacy of Lung Stereotactic Body Radiation Therapy for Surgical Staple Line Recurrences

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Purpose

Surgical resection remains the gold standard for stage I non-small cell lung cancer (NSCLC) and is often employed for the diagnostic/therapeutic management of solitary metastases. Despite the low incidence of local recurrences (LR) along surgical staple lines, the ideal strategy for managing tumor recurrences of the staple lines have not been well established. We updated our initial report on the safety and efficacy of lung SBRT as a single modality salvage treatment strategy for staple line recurrences (SLR) following surgical resection.

Method

We identified 15 patients from an IRB-approved prospectively maintained database who were treated for SLR after surgical resection for the management of stage I NSCLC or oligometastases. These patients were treated from 5/2012 to 6/2018. Ten patients had a primary, NSCLC and five patients had oligometastases. We calculated the median time from surgery to SBRT treatment, median follow up (MFU), and crude rates of local (defined as in-field and along the staple line), regional (defined as out-of-field lobe/lung and/or regional lymph nodes), and distant (contralateral thorax or distant systemic spread) control. Dosimetric information including Planning Treatment Volume (cc), total radiation dose, dose per fraction and SBRT treatment planning techniques were also evaluated. Common terminology criteria for adverse events version 4 (CTCAEv4) were used to measure treatment-related toxicities.

Results

Median age at the time of treatment was 67 years (range 50-86 years). The median time from LR to initiation of SBRT was 17 months (range 3-75 months). The median total SBRT dose was 54 Gy (range 45.0-60.0 Gy) with median dose per fraction of 11.50 Gy (range 4.5-18.0 Gy). A simultaneous integrated boost (SIB) technique, which included the entire staple line with a tumor boost, was employed in 4/15 (27%) cases. The median PTV for all patents was 17.90 cc (range 9.40-47.10 cc). The median combined PTV of patients treated with an SIB technique including the staple line was 22.02 cc (range 15.43-29.08 cc). With MFU of 25 months (range 5-67 months) one patient (6.7%) experienced a local failure at the staple line, for a crude local control rate of 93.3%. Three patients with NSCLC (20.0%), including the one local failure, failed regionally (in the lung, outside of the SBRT field) and distantly at 8, 9 and 36 months respectively. Of the 12 patients (75%) with toxicity data available, only grade 1 toxicities were reported (fatigue (1), dyspnea (1), pneumonitis (2), or chest wall pain (1)).

Conclusions

Salvage SBRT for surgical staple line failures appears to be very efficacious and well tolerated (no grade 2 or above toxicities). Further investigation is needed to determine the optimal dose and treatment volume for this...
Impact of Patient Stage and Disease Characteristics on the proposed Radiation Oncology Alternative Payment Model (RO-APM)

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Purpose

The proposed Radiation Oncology Alternative Payment Model (RO-APM) released on July 10, 2019 represents a dramatic shift from fee-for-service (FFS) reimbursement in radiation therapy (RT). Limited clinical information was used in the development of the RO-APM. This study compares historical revenue to the RO-APM and quantifies the impact that disease stage, modality, and disease subcategory have on reimbursement.

Method

FFS Medicare reimbursements were determined for patients undergoing RT at Mayo Clinic Rochester and Florida from 2014-2016. Disease categories and payment episodes were defined as per the RO-APM. Average RT episode reimbursements were reported for each site and stratified by stage, disease subcategory, and modality. Comparisons with RO-APM reimbursements were made via descriptive statistics.

Results

5,279 patients were identified and 3,964 (75%) categorized per the RO-APM. The most common diagnoses were breast (25%), lung (15%), prostate (12%), and head and neck (HN) (12%). RO-APM reimbursements and historical reimbursement differed by disease category most for bladder cancer (-37%), cervical cancer (-23%), head and neck cancer (-17%), liver cancer (+71%), breast cancer (+60%), and uterine cancer (+50%). Historical reimbursement was significantly higher with advanced stage (Stage III vs. Stage I), most prominent for breast cancer (110%), lung cancer (80%), and prostate cancer (68%). The proposed RO-APM significantly under-reimbursed for proton therapy by -17% overall, a difference most significant in breast (-39%), CNS (-29%), and Upper GI (-24%) cancers.

Conclusions

The RO-APM will result in significant reductions in reimbursement for cancers that are more common in minorities, rural populations, and socioeconomically disadvantaged populations which could further reduce access for this vulnerable population. The RO-APM will result in dramatic reductions in reimbursement for proton therapy and likely other advanced technologies.

Socioeconomic/ethical issues/health outcomes research

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Utilization of post-mastectomy radiation therapy in breast cancer patients treated with neoadjuvant chemotherapy

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Purpose

Neoadjuvant chemotherapy (NAC) is a widely utilized treatment approach for breast cancer. In absence of prospective data, tools such as a nomogram developed from the results of NSABP B-18 and B-27 (Mamounas et al, JCO 2012) are useful to assess risk of locoregional recurrence in patients treated with NAC and identify patients who might benefit from post-mastectomy radiation therapy (PMRT). Our study is the result of a prospective clinical registry of breast cancer patients who received NAC followed by surgery with the goal of observing PMRT treatment patterns impacted recurrence risk.

Method

Patients with clinical stage I-III breast cancer treated with NAC and surgery +/- radiation were enrolled on a prospective registry from 2013-2018 at our institution. Low-risk patients were defined as those with clinical Stage II disease and ≤10% locoregional relapse risk defined by the Mamounas
nomogram. High-risk patients were defined as those with clinical Stage III disease or clinical Stage II with >10% locoregional relapse risk.

Results

A total of 43 patients receiving NAC were enrolled with median follow up of 31.9 months after surgery. Median age of patients was 46 years. 24 (55.8%) patients had Stage II disease and 19 (44.2%) patients had Stage III disease. Of 43 patients enrolled on the registry, 35 underwent NAC followed by mastectomy. Of these, 27 (77.1%) underwent PMRT. Of 35 patients who received NAC followed by mastectomy, 8 were defined as low risk and 27 were defined as high risk of LRR based on the above definition. In the low risk group a total of 6 patients (75%) received PMRT. In the high risk group, 21 patients (77.8%) received PMRT. Among 17 clinical stage III patients, 16 (94%) received PMRT. Of the 18 clinical Stage II patients, 10 were classified as high risk and 8 were classified as low-risk. In stage II patients, 5 (50%) of the high risk patients were treated with PMRT and 6 (75%) of the low risk patients were treated with PMRT. There were 5 recurrences in all high-risk patients (18.5%) and 1 recurrence in low-risk patients (12.5%). Relative risk of recurrence in the high risk group compared to the low risk group was 1.48 [95% CI: -0.52 to 3.48]. Of those who underwent PMRT, 5 (18.5%) patients experienced any recurrence. In patients who didn’t receive PMRT there was one recurrence (12.5%).

Conclusions

Our study shows that patients received a similar rate of PMRT irrespective of predicted risk. This was driven by treatment patterns in patients with Stage II disease, particularly a relatively low rate of PMRT in high risk patients. Future research should focus on the rationale for using PMRT in patients treated with NAC and validation of risk prediction models of LRR after NAC for breast cancer.

Categories

Clinical investigations

Radiotherapy for Adult Soft Tissue Sarcomas of the Head and Neck

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Purpose

Surgery followed by postoperative radiation therapy (RT) is the standard of care for soft tissue sarcomas (STS) of the head and neck that are high-grade or have close or positive margins. Here we report the outcomes of this rare tumor in adults.

Method

This is a retrospective review of adult patients with head and neck STS treated with RT between 1981 and 2017. All patients who were > 19 years old with STS of the head and neck, excluding rhabdomyosarcoma, angiosarcoma and Ewing tumors, were included in this study. Toxicity was graded using CTCAE version 4.

Results

34 patients with head and neck STS treated with postoperative RT (33) or primary RT (1) met the inclusion criteria. The median age at diagnosis was 45 years (range, 20 to 83). Overall, 37% had T1 tumors, 50% had high-grade histology (grade 3), and 26% had microscopically positive margins. The median RT dose was 65 Gy to the primary site; 29% received elective nodal irradiation. The median follow-up for living patients was 16.6 years (range, 0.6-30 years) for living patients. At 5 years and 10 years, the local control rates were 88% and 82%, the regional control rates were 97% and 97%, the freedom from distant metastases rates were 100% and 100%, the cause-specific survival rates were 88% and 82%, and the overall survival rates were 85% and 69%. Two patients (6%) developed late grade 3+ complications.

Conclusions

Our study demonstrates that surgery and RT for STS of the head and neck cures 82% of patients at 10 years. Local failure is the most common form of recurrence.

Categories

Clinical investigations

Advanced - Stage Hypopharyngeal Carcinoma management: A Retrospective Review of 25-years of experience.

Toms Vengaloor Thomas, Mary Nittala, Eldrin Bhanat, Teessa Perekattu Kuruvilla, Anu Abraham, Satyaseelan Packianathan, Srinivasan Vijayakumar
The two treatment groups were similar in terms of for age, gender, ethnicity, alcohol status, N staging, and subsites, but were significantly different for smoking status \( (p=0.035) \) and T staging \( (p=0.024) \).

The median follow-up was 17 months. The median survival of overall cohort was 26 months and 5-year overall survival was 25.5\%. The median survival was found to be significantly better for the surgery group as compared to definitive chemoradiotherapy group (43 months vs 16 months, \( p=0.049 \)). The 5-year overall survival (OS) (41.5\% vs 18.5\%, \( p=0.049 \)) and disease-free survival (DFS) (75.3\% vs 56\%; \( p=0.029 \)) were significantly better for patients in surgery group compared to chemoradiotherapy group. On multivariate Cox-regression analysis, lymph nodal status (HR= 1.27, CI: 1.00-1.62, \( p=0.047 \)) and chemoradiation treatment (HR= 1.82, CI: 1.00-3.29, \( p=0.048 \)) were associated with higher risk of mortality.

In our single institutional experience of advanced hypopharyngeal carcinoma management, the 5-year overall survival rate was found to be 25.5\% and is poorest among head and neck cancers. The patients with advanced hypopharyngeal cancer treated with surgery followed by adjuvant radiation or chemoradiation have significantly improved overall survival compared to those treated with definitive chemoradiotherapy. Further research warranted for early detection and better treatment to improve the cure rate in hypopharyngeal carcinoma patients.

References


Categories

Socioeconomic/ethical issues/health outcomes research

Proton FLASH: the fastest path to human treatment

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Purpose

FLASH therapy refers to radiation dose delivered at dose rates that are greater than 40 Gy/s. FLASH therapy holds the potential to dramatically reduce normal tissue toxicity while preserving equitoxicity to tumor tissue as compared to conventional (CONV) irradiation. However, many of the early preclinical FLASH experiments have been done using electrons or X-rays. There are significant barriers to clinical translation using these technologies, as the beam properties...
of these preclinical systems may only be suitable for a limited subset of tumors such as superficial lesions. Proton FLASH represents the fastest method to human translation because of its ability to treat deep-seated tumors. Here, we describe our results using proton FLASH to determine its impact on normal tissue toxicity and tumor efficacy in preclinical models. In addition, we discuss important considerations for the translation of this important new therapy into the clinic.

Method

Irradiations were performed on a clinical Varian ProBeam system in research mode with pencil beam scanning at 250 MeV including a modified dose monitoring system. A C57Bl/6 mouse model was used to determine the impact of proton FLASH on normal lung tissue toxicity. FLASH (40 Gy/s) or CONV (1 Gy/s) radiation was administered to these animals, followed by histopathological analysis of normal tissue toxicity including lung fibrosis. Separately, a Lewis Lung Carcinoma cell line was injected into the lungs of C57Bl/6 mice, and the thoracic region was irradiated with FLASH (40 Gy/s or 100 Gy/s) or CONV radiation. Survival was monitored to determine the effect of FLASH on tumor control.

Results

A 23% reduction in overall fibrosis severity was observed at 34 weeks post irradiation in healthy mouse lung treated with 17.5 Gy FLASH radiation versus 17.5 Gy CONV radiation along with improved survival for FLASH treated mice. Further, both 40 Gy/s and 100 Gy/s of FLASH irradiation led to equivalent tumor control as CONV radiation.

Conclusions

Preclinical results indicate that proton FLASH is a promising alternative to CONV radiation and may allow us to widen the therapeutic window. As efforts continue towards human translation, several key challenges must be addressed. First, it is important to verify the safety of this new technique and ensure that dosimetry is correctly performed using multiple methods to confirm the radiation dose delivered. Further, the definition of dose rate is key to ensuring consistency across platforms and dose delivery techniques which will bolster the validity of preclinical experiments as we move towards human FLASH trials. Finally, greater understanding of the biological parameters within which FLASH is effective will improve the biological efficacy of FLASH and enable the widest possible cohort of patients to benefit from this potentially groundbreaking research technology.

Categories

Translational science

Physician-Predicted Prognosis and Utilization of Palliative Radiation Therapy at the End-of-Life- An Audit of a Large Cancer Center Network

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Purpose

Palliative radiation therapy (PRT) is important for symptom management in patients with advanced cancer. Studies have shown that longer courses of RT (LCRT) are commonly used for PRT, adding to the socioeconomic hardships in this vulnerable population. Our clinical pathways (CPs) capture physicians’ prognostication of patients’ expected survival at time of consultation along with the recommended RT course. In our CPs, the preferred palliative treatment is either single or short course fractionation. We evaluated utilization rates of LCRT at the end-of-life within our integrated cancer network.

Method

A retrospective review was conducted on patients who were evaluated for PRT between January 2017 to August 2019 and died within 90 days of consultation. The predicted prognosis, intended RT course, RT technique, and treatment completion rates (CRs) were captured. Binary logistic regression was used to identify predictors for treatment completion and utilization of LCRT, defined as ≥10 fractions. Potential predictive factors included: predicted prognosis, physician’s number of years in practice (<15 vs ≥15 years), type of metastasis (bone, brain, and non-brain/bone), time to death after consultation (0-30, 31-60, and 61-90 days), patient’s age (≤60 vs >60 years), primary disease site, demographic factors (sex, race, and
ethnicty), and practice setting (community vs. academic).

Results

We identified 1,608 patients who died within 90 days of consultation. Most patients had a lung primary (51.6%), were >65 years of age (57.9%), and were treated for bone metastases (45.8%). A total of 570 patients (35.4%) were predicted to live beyond one year. Stereotactic radiosurgery (SRS) was recommended for 11.8%, 17.4%, and 20.2% of patients dying 0-30, 31-60, and 61-90 days from consultation, respectively (p<0.0001). On multivariate analysis (MVA), patients evaluated at academic sites (p<0.0001, OR 0.08; 95% CI 0.05) were more likely to recommend LCRT, while physicians with ≥15 years of practice (p=0.04, OR 1.31; 95% CI 1.01) were less likely to recommend LCRT, while physicians with ≥15 years of practice were more likely to recommend LCRT (p=0.09). On multivariate analysis (MVA), patients evaluated at academic sites (p<0.0001, OR 0.33; 95% CI 0.25-0.42) and patients with bone or non-brain/bone metastases (p<0.0001, OR 0.08; 95% CI 0.05-0.12 and OR 0.20; 95% 0.13-0.31, respectively) were less likely to be recommended LCRT, while physicians with ≥15 years of practice were more likely to recommend LCRT (p=0.04, OR 1.31; 95% CI 1.01-1.70).

Excluding 250 patients recommended SRS, LCRT was recommended for 58.8%, 62.8%, and 66.2% of patients dying 0-30, 31-60, and 61-90 days from consultation, respectively (p=0.04). On MVA, patients recommended LCRT were less likely to complete treatment than those recommended conventional single-fraction RT (p<0.001, OR 0.06; 95% CI 0.03-0.12).

Conclusions

Utilization of LCRT was similar irrespective of survival after consultation. Despite guidelines and pathway recommendations, LCRT was commonly used at end-of-life with low CRs. A better predictive survival model is needed to minimize treatment related socioeconomic hardships and improve quality of care in this vulnerable population.

Categories

Clinical investigations

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Does a bioabsorbable device placed at the time of breast conserving surgery improve breast cosmesis?

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Purpose

Breast tissue removed during lumpectomy can alter the appearance of a woman’s breast. A bioabsorbable 3-dimensional device (BD) can be sutured into the resection bed to fill the surgical cavity created from the lumpectomy. These devices come in various shapes and sizes to fit the cavity. Unlike surgical clips which can vary in usage, number, and location based on surgeon’s discretion, the BD has 6 titanium clips imbedded in a uniform array. These titanium clips also serve as a fiducial for radiation treatment planning (RTP) and imaging. We hypothesize the using a BD at the time of lumpectomy will result in better breast cosmetic outcomes and smaller radiation target volumes than patients without BD.

Method

We reviewed all patients who underwent whole breast irradiation (WBI) with and without planned oncoplastic reconstruction after breast conservation surgery (BCS) from the time BD became available at our institution on 1/2016 to 12/2017. All patients were treated in the prone position using 3DCRT to 40-50 Gy to the breastPTVeval at 2-2.7Gy/fraction with 99% receiving 8-16Gy at 2Gy/fraction lumpPTVeval boost. Physician-reported cosmetic outcome at 6- and 12-months were categorized using the NRG-RTOG Breast Cosmesis Scale (excellent/good (EG), fair/poor (FP)). Breast cosmesis at 6- and 12-months and median LumpGTV volume were analyzed using the Wilcoxon signed-rank test and descriptive statistics for other variables was performed.

Results

We treated 246 women from 1/2016-12/2017 with prone WBI after BCS. There were 129 (52.4%) right-sided and 14.6% DCIS, 67% Stage I, 15% Stage II, 0.4% Stage III, and 3% ypT0. Median LumpGTV is 24cc BD (n=56), 31.2cc clips (n=95), and 16.9cc no markers (n=95) (p=0.0004). Overall EG breast cosmesis at 6-months was 98% and 12-months was 96.7%. EG cosmesis at 6- and 12-months was similar for patients with BD (98%, 96.5%), clips (99%, 97%), and no marker (97%, 97%). When excluding 7 women with planned oncoplastic surgery, no difference in breast cosmesis was found overall or in any subgroup.

Conclusions

For patients with early-stage breast cancer treated with lumpectomy and WBI, after RTP the median LumpGTV
volumes in patients with BD were smaller than clips and larger than those no markers. However, 6- and 12-month excellent/good cosmesis was high for all patients regardless of presence of cavity marker. Future studies include long-term outcomes.

References


Categories

Clinical investigations

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Outcomes from Post-Mastectomy Radiation Therapy (PMRT) after Implant-based Reconstruction for Breast Cancer

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Purpose

Post-mastectomy radiation therapy techniques are often-field based rather than volume based and by including the implant, exposes a greater amount of normal tissue to radiation. Patients with immediate reconstruction with implant are often prescribed an over dosage of radiation therapy. The purpose of this research was to identify outcomes in patients treated with post-mastectomy radiation therapy after implant based reconstruction for breast cancer.

Method

We retrospectively reviewed the records of 69 patients treated with adjuvant radiation therapy following mastectomy with immediate reconstruction and implants treated at Mayo Clinic Florida from 2000 to 2019. Demographic and treatment outcomes data were collected. Survival was estimated using a Kaplan-Meier survival curve.

Results

The median age of patients treated with PMRT was 47 years. Invasive ductal carcinoma was seen in 85% of patients, with 46% and 49% of tumors occurring in the right and left breasts, respectively. Approximately 35% of patients were treated with chemotherapy. With a median follow up of 49 months, the overall survival was 96%. Patients with tissue expanders had a longer time from date of diagnosis to first radiation treatment compared to those without a tissue expander (226 days vs 206 days, p=0.021).

Conclusions

Post-mastectomy radiation therapy after implant-based reconstruction was found to be an effective treatment options for those patients that required radiation therapy following mastectomy and immediate reconstruction. Notably, patients with tissue expanders experienced a greater time to treatment, which may influence oncologic outcomes. Future studies can investigate the influence of this delay in outcomes.

Categories

Clinical investigations

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STK11 Mutation Predicts Rapid Treatment Failure Following Ablative Radiotherapy for Early Stage NSCLC

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Purpose

Patients with medically inoperable early stage NSCLC are frequently treated with ablative radiotherapy. While local control is excellent, out-of-field recurrence remains a challenge. There is limited data regarding molecular predictors of recurrence in this setting as many are treated without pathologic confirmation. We utilized a validated next-generation sequencing (NGS) technology to identify pathogenic mutations associated with recurrence.

Method

We retrospectively reviewed all early stage NSCLC patients who received radiotherapy at our institution and underwent NGS with OncoPlus, a 1212-gene genomic sequencing assay. Patient and treatment characteristics and disease outcomes were collected. The association of mutations with recurrence was assessed.

Results

19 patients with medically inoperable, node-negative NSCLC underwent OncoPlus between 2017-2019. Median age was 74, 12 were female, and median smoking was 30 pack-years. 95% had adenocarcinoma. AJCC 8th edition stage breakdown was: IA (n=9), IB (n=4), IIA (n=1), and IIB (n=5). Radiotherapy was delivered as SBRT (50-55 Gy in 5 fractions [n=15]) or
hypofractionated RT (70 Gy in 10 fractions [n=4]). Median follow-up was 16 months (range, 7 – 42), with 2 patients dead. 9 experienced recurrence, with distant failure a component in 8/9. Crude local control rate at 2 years was 89%.

17/19 patients underwent OncoPlus of their primary; 2 had OncoPlus of a recurrence. KRAS, TP53, and KRAS/TP53 co-mutations were present in a similar proportion of patients with recurrence and those without (56% vs. 50%, 56% vs. 40%, and 33% vs. 20%, respectively). By contrast, serine/threonine kinase 11 (STK11), a tumor suppressor mutated in 1/3 of NSCLC that predicts resistance to anti-PD-1 immunotherapy, was differentially mutated. 57% of patients with STK11 mutations vs. 0% without STK11 mutations experienced early treatment failure (defined as recurrence within 6 months) (p=0.004); this result held when excluding OncoPlus performed at recurrence (60% vs. 0%, p=0.006). Using the Kaplan-Meier method, median PFS was 30.0 months in the STK11 wild-type group vs. 6.5 months in STK11 mutants (p=0.002). Multivariate Cox proportional hazards analysis including stage demonstrated STK11 mutation was independently associated with an 8.6-fold increased risk for progression (p=0.004).

Conclusions

In a cohort of medically inoperable, early-stage NSCLC patients treated with ablative radiotherapy, NGS identified STK11, an established marker of immunotherapy resistance, as a putative predictor of failure. This raises the possibility of immune exclusion as a driver of recurrence in early stage NSCLC and suggests a need for sequencing of tissue or circulating DNA to identify a higher risk subset that might benefit from adjuvant therapy. These results should be validated in a larger cohort.

References


Categories

Clinical investigations

Application of \(^1\)H MRI to the assessment of regional changes in pulmonary perfusion after SBRT for early stage non-small cell lung cancer

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Purpose

Radiation therapy plays a critical role in the management of thoracic malignancies. However, treatment is complicated by the risk for radiation-induced lung injury (RILI). Functional imaging of regional pulmonary ventilation and/or perfusion has emerged as a promising approach to studying radiation-induced changes in pulmonary function. Recently, techniques have been developed for quantifying regional pulmonary perfusion using standard \(^1\)H magnetic resonance imaging (MRI) platforms. The purpose of this study is to determine whether \(^1\)H MRI can detect radiation-induced changes in pulmonary perfusion.

Method

For this pilot study, the population was limited to patients undergoing definitive stereotactic body radiation therapy (SBRT) for early-stage non-small cell lung cancer to eliminate potentially confounding effects of systemic therapy. Briefly, patients underwent MRI scans prior to and 6 weeks following SBRT. Proton density was measured using a fast multi-echo gradient-echo sequence, and perfusion was measured using arterial spin labeling (ASL-FAIRER). Images were reconstructed with 1.56x1.56mm in-plane resolution of and 15mm slice thickness. The imaging volume was limited to the ipsilateral (treated) lung. Images were acquired at functional residual capacity while the patient performed a short breath hold. To correlate changes in regional perfusion with radiation dose, radiation treatment plans from 4D CT simulation scans were registered with the MR images using affine CT simulation. For quantification of dose effect, radiation isodose levels were binned as low (<5Gy), moderate (5-60Gy), high (>60Gy), or within the ITV, with dose expressed in terms of BED to account for variation in fractionation. Regional perfusion measurements at each timepoint were normalized by mean lung perfusion to account for variation in cardiac output across scans. Statistical significance was assessed with the Wilcoxon signed-rank test.

Results
Three patients have completed pre-treatment and 6-week post-treatment scans to date. None experienced clinical pulmonary toxicity at the 6-week timepoint. A trend toward a relative increase in perfusion in the moderate-dose region was observed, with changes of -52±4% and 23±6%, in the low-dose and moderate-dose regions, respectively (mean+/standard deviation). Perfusion also increased on average in the high dose and ITV regions, albeit more variably, with changes of 17±25% and 15±26%, respectively. Likely due to small sample size, none of the measured changes was statistically significant.

Conclusions

Small sample size limits our conclusions at this time; however, early results are consistent with subacute increased perfusion in the radiated lung after SBRT, potentially due to sub-clinical post-treatment inflammation. Feasibility of using 1H MRI to measure the effect of radiation on regional pulmonary perfusion appears promising, and increasing sample size will allow for firmer conclusions to be drawn. Planned follow up imaging at 6 months will assess whether the observed perfusion changes persist beyond the subacute post-treatment period.

References


Categories

Physics/technology

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Intracranial Control and Survival Outcomes with Radiosurgery Treatment of Brain Metastases Detected Prior to and During Immune Checkpoint Inhibition Therapy

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Purpose

The use of immune checkpoint inhibitor therapy has led to increased control of systemic disease and improved survival among patients with metastatic disease across multiple different solid cancers. As immune therapy has variable success in controlling intracranial metastatic disease, stereotactic radiosurgery (SRS) can play an important role in controlling overall disease progression. We hypothesize that patients who develop brain metastases while on immune checkpoint inhibition have worse intracranial control and survival relative to those who develop brain metastases at or before initiation of immune therapy, and seek to describe these outcomes in those two groups.

Method

Patients with brain metastases treated with SRS and immune checkpoint inhibition at our institution between 2012 and 2018 were identified by retrospective review, and were stratified by whether brain metastasis developed while on immune therapy vs prior to initiation of immune therapy, and by control of extracranial metastatic disease at time of SRS. Intracranial progression-free survival (PFS) and overall survival (OS) from time of SRS were plotted using the Kaplan-Meier method, and compared using the log-rank method.

Results

A total of 53 patients treated with immune checkpoint inhibition and with brain metastasis treated with SRS were identified. Of these, 17 (32%) were on immune checkpoint at time of brain metastasis diagnosis, and 15 (28%) had isolated brain metastasis in the setting of controlled systemic disease. In comparing those who developed intracranial metastasis while on immune therapy vs. before start of therapy, no significant difference was seen in intracranial PFS (6-month PFS 59% vs 54%, p=0.3) or OS (6-month OS 71% vs. 78%, p=0.22). Twenty-four month OS was lower in the group who developed brain metastasis while on immune therapy (22% vs 41%), though the ability to draw conclusions about differences was limited by small number at risk in each group (6 and 13 patients, respectively). A trend toward worse OS was seen (median 12.1 vs. 18.2 months, p = 0.1) among patients who had uncontrolled systemic disease vs. those with intracranial metastasis alone.

Conclusions

Outcome of aggressive management of brain metastasis with radiosurgery is favorable for patients receiving immune checkpoint inhibitor therapy even when brain metastasis develop during immune checkpoint inhibitor therapy, although survival may be inferior for those with evidence of systemic disease rather than isolated brain metastasis. Additional follow-up is needed to assess very long term survivorship.

Categories

Physics/technology

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Intracranial Control and Survival Outcomes with Radiosurgery Treatment of
Factors influencing patient experience ratings in radiation oncology

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Purpose

Patient experience has been increasingly emphasized to ensure patient-centered healthcare. Patient experience surveys have been adopted as measures to evaluate physicians and guide value-based reimbursement after comparison to historical benchmarks. This is particularly relevant to radiation oncologists given the proposed mandatory implementation of the Radiation Oncology Alternative Payment Model, which includes withholdings that incorporate patient experience data. However, studies suggest that patient experience scores can reflect inherent biases, displaying a potential need for analytic approaches accounting for these factors. This study will explore patient-, physician-, and healthcare environment-related factors that influence patient experience scores.

Method

A retrospective review of patient experience survey data will be conducted for patients evaluated and treated by the Mount Sinai and Memorial Sloan Kettering Cancer Center radiation oncology departments from 2017 to 2019. The primary outcome is response to the survey item querying likelihood to recommend the practice to others. Secondary outcomes include responses to items related to patient experience of the physician including friendliness, explanations about condition, and perceived concern. Patient clinical information (e.g. disease characteristics, treatment type) will be obtained from medical records. Provider and healthcare environment-related information (e.g. physician gender, years in practice, and average case mix risk; and practice setting and volume) will be obtained via administrative and medicare data. Patient experience scores will be grouped by patient-, physician-, and healthcare environment-related factors. Scores will be compared across groups and multivariable analyses will be performed to assess independent predictors for high patient experience scores.

Results

Preliminary data yielded 11332 surveys completed for 48 radiation oncologists (8 MSH, 40 MSKCC), with a median of 186 surveys per physician (IQR 38-347). The physician male-to-female ratio was 17:7. Most physicians had 0-9 (29.2%) or 10-19 (35.4%) years in practice. The mean summary score for likelihood to recommend practice was 96.8% (SD 3.5). The mean summary score was 97.1% (SD 2.8) amongst males and 95.8% (SD 4.9) amongst females. The study is ongoing. Analysis of response-level patient experience scores and patient-, provider-, and healthcare environment-related data will be presented at the conference.

Conclusions

Expected findings will provide greater insight into factors influencing patient experience ratings in radiation oncology, which has practical implications related to reimbursement models and overall quality of care. This may aid further development of survey tools and interpretation processes to increase parity and accuracy of patient experience evaluations.

Categories

Socioeconomic/ethical issues/health outcomes research

Patterns of Failure in Early-Stage Low-Risk Pediatric Hodgkin Lymphoma: A Secondary Analysis of COG AHOD 0431

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Various treatment strategies exist for early-stage low-risk pediatric Hodgkin Lymphoma (pHL), including response-adapted approaches in patients who respond favorably to initial chemotherapy. Low-risk pHL is highly curable in most children; however, there is a significant risk of late toxicity with approaches that utilize upfront chemotherapy and radiation therapy (RT). Often, patients who relapse with a low disease burden after chemotherapy alone can be successfully salvaged with low-dose chemotherapy and involved-field RT (IFRT), sparing upfront RT in low-risk disease.

In an effort to de-escalate treatment, AHOD0431 examined whether reducing upfront treatment, by using a response-based approach, could maintain overall survival while reducing late toxicity. Patients with stage IA and IIA pHL were initially treated with chemotherapy alone. Patients undergoing a complete response (CR) by both PET3 (Deauville 1 or 2 was negative but no scores were assigned at the time of the study) and CT (80% or greater reduction in PPD) received just 3 cycles of AVPC (adriamycin, vincristine, prednisone, cyclophosphamide) chemotherapy, while patients with a partial response (PR) or stable disease received 21 Gy of IFRT. While the study did not demonstrate that patients at the end of chemotherapy could safely have omitted RT, the study did show that PET/CT after 1 cycle (PET1) of chemotherapy was prognostic for outcomes.

The purpose of our study is to examine patterns of failure in AHOD 0431 and whether PET1 and/or PET3 (PET/CT after 3 cycles of chemotherapy) predict for not only relapse but relapse within a slowly responding site, or if they are prognostic for relapse elsewhere. The importance of this study is to understand whether there might be value in delivering higher doses of radiation to PET-positive sites (based on PET1 or PET3).

Method

For the 52 patients who relapsed on AHOD 0431, PET1, PET3, radiation treatment plans (if radiation was received), and PET scan on relapse will be reviewed. Sites of recurrence in relationship to prior imaging and, if applicable, to RT fields, will be categorized as follows: in-field within a PET1-positive site, in-field within a PET3-positive site, in-field within the original disease site but outside of the PET1- or PET3-positive site, or out-of-field. To do this study, we will travel to IROC Rhode Island to review the 52 patients who relapsed among the 275 patients enrolled in the study.

Results

The relapse rate in the study population was 19%. After excluding 5 patients who underwent a gallium scan and 2 whose charts were incomplete, 45 patients remained for evaluation. Overall, 76% of patients who relapsed did not receive upfront RT and 24% of patients who relapsed did receive upfront RT.

Conclusions

We will report the conclusions at the meeting.

Categories

Clinical investigations

Metastatic Lung Cancer and Definitive Local Therapy with Radiation: Clinical and Treatment Related Factors Associated with Improved Outcomes in Oligometastatic Disease

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Purpose

The standard of care therapies for metastatic non-small cell lung cancer (NSCLC) are systemic approaches including chemotherapy, immunotherapy, or targeted therapy. However, phase II data (NCT01725165) suggests that local consolidative therapy improves progression-free survival (PFS) and overall survival (OS) in oligometastatic NSCLC compared to systemic therapy alone. Few studies have identified clinical patient factors that may predict which patients will benefit most from consolidative radiotherapy (cRT). In this study, we report a clinical prediction model of PFS in patients with oligometastatic NSCLC treated with definitive radiotherapy.

Method
Patients with metastatic NSCLC treated with definitive radiotherapy to metastatic sites and primary tumor between 2008 and January 2019 were identified. Oligometastases were defined as < 3 sites of disease not including the primary tumor. Patients with localized disease who subsequently developed distant recurrence were included if there were < 3 sites of distant disease treated with definitive intent. PFS and OS were calculated from the end of radiotherapy using Kaplan-Meier methodology. Univariable Cox proportional-hazards model was used to compare outcomes with demographic and clinical characteristics. Least absolute shrinkage and selection operator (LASSO) method was used to select features that were most significant and then build a predictive nomogram model for selection of patients most likely to benefit from cRT.

Results

Our group abstracted 2743 definitively dosed radiation events from an institutional database. A final cohort of 89 patients with oligometastatic NSCLC that met inclusion criteria was analyzed. At the time of treatment, the median age was 63 years (33-89), 53.9% of patients were female (n=48) and 70.8% were Caucasian (n=63). Adenocarcinoma (79.8%) was the most common histology. Solitary metastasis occurred in 82% of patients (n=73) with 37% having metastasis in the brain (n=33). Median follow up time was 15.7 months (0.35 – 116.7). Median PFS and OS was 7.91 and 36.7 months, respectively. On univariate analysis, stage IV at diagnosis (HR 1.71, 95% CI 1.02 – 2.88, p=0.04) was significantly associated with a worse PFS. Male gender (HR 1.82, 95% CI 0.99 – 3.82, p=0.05), squamous histology (HR 4.08, 95% CI 1.97 – 8.47, p<0.001), and hypofractionated therapy (HR 5.20, 95% CI 2.05 – 13.20, p<0.001) were associated with worse OS. On nomogram modeling, the following were selected to drive improved PFS: intracranial metastases (p=0.09), intrathoracic metastases (p=0.006), and targetable mutations (p=0.17). The PFS for patients with these characteristics was 11.2 months (n=24) vs. 7.65 months (n=65) for those who did not.

Conclusions

A clinical nomogram model has identified a subset of patients in which cRT for oligometastatic NSCLC extends PFS. This model may have clinical implications in delaying the initiation of 2nd or 3rd line systemic therapies, which often have poor response rates. Further randomized data is needed to validate these findings.

Categories

Clinical investigations

Repeat Stereotactic Radiosurgery for In-field Recurrence of Brain Metastases Previously Treated with Radiosurgery

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²Mehmet Ali Aydinlar Acibadem University, Istanbul, Istanbul, Turkey

Purpose

Stereotactic radiosurgery (SRS) is the preferred initial treatment option in patients with limited number of brain metastases. However, in case of relapse after initial SRS the optimal salvage treatment is not well defined. While efficacy of SRS has been demonstrated in several prior studies, tumor control and treatment related complications, particularly symptomatic radiation necrosis (RN), remain as obstacles for wider adoption of repeat SRS for asymptomatic brain metastases. We sought to determine the effectiveness of repeat SRS for in-field recurrent brain metastases.

Method

We conducted a retrospective review of 217 patients with 414 brain metastases treated with SRS from 2009 to 2018 at our institution. Patients who underwent repeat SRS for local tumor progression following prior SRS were included in this analysis. Post treatment MRIs were reviewed for treatment response which was defined as complete, partial, or no response. RN was diagnosed according to a combination of criteria, including appearance on serial MRI scans, MR spectroscopy (MRS), and histology. Patients requiring therapy or developing any new neurologic complaints were scored as having symptomatic RN.

Results

We identified 27 brain metastases treated with repeat SRS in 13 patients.
The median age, target volume, coverage, and normalization was 54 years (range, 30-71 years), 0.96 cm³ (range, 0.10-15.0 cm³), 98% (range, 92.7-100%), and 84% (range, 77-89%), respectively. Whole brain radiation was received by 67% of the patients either before or after initial SRS. The initial and repeat median SRS dose was 20 Gy (range, 12-30 Gy) in 1 to 5 fractions. Fourteen lesions (52%) demonstrated complete response, 6 (22%) partial response, and 7 (26%) no response to repeat SRS. Symptomatic RN occurred in 5 patients (38.5%) and 8 total lesions (29.6%), and was treated with steroids, bevacizumab, or surgery with 75% complete response. The median overall survival was 15.1 months from the date of initial SRS and 6.3 months from the date of repeat SRS.

Conclusions

Repeat SRS is a feasible treatment option for patients with in-field recurrence of brain metastases leading to long term survival and good local control. The increased risk of symptomatic RN with repeat SRS can be used to guide the decision-making for patients with in-field recurrence.

Categories

Clinical investigations

Automated Segmentation of Multimodal MRI/MRA Images for Cerebral AVM SRS
Treatment Planning – A Deep Learning Approach

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Purpose

Stereotactic radiosurgery (SRS) is a standard treatment for unresectable arteriovenous malformations (AVMs). Accurate AVM nidus delineation is critical for treatment planning. However, the AVM nidus can be difficult to delineate as it requires interpretation across several imaging sequences. Our objective was to use deep learning artificial intelligence to automatically segment cerebral vascular structures from multi-modal magnetic resonance images (MRI), combining information across three high-resolution MRI modalities to produce high-resolution vascular maps for SRS planning.

Method

Subjects: 21 patients were included. Spetzler-Martin Grade ranged from I-V. Ruptured, intact, and partially embolized lesions were included. 15 cases were used for training and 6 for validation.

Imaging: Patients underwent MRI/MRA, including 3D time-of-flight (TOF), contrast enhanced 3D fast spoiled gradient echo (FSPGR), and 3D T2 sequences. TOF, T2, and FSPGR images were reconstructed with resolutions of 0.45/1mm, 0.5/0.9mm, and 0.49/1mm (axial-plane/slice), respectively. FSPGR and T2 volumes were registered to TOF volumes and re-sampled to the TOF resolution.

Labeling: Voxel-scale labels were generated with combination of automated and manual labeling. Briefly, samples of structures of interest (arteries, veins, embolized vessels, brain parenchyma, CSF) were manually labeled, as was the extracerebral volume. Images and labels were imported into MATLAB where a support vector machine-based algorithm generated labels for the remainder of the image volume. The label volumes were then meticulously edited slice-by-slice to correct clearly mislabeled voxels. These labels were used to train a neural network to predict voxel-scale labels from multimodal image volumes. The training set contained 2733 unique image slices. Augmentation by L/R reflection of nidus-containing slices yielded an additional 789 slices.

Neural Network Implementation: A 2D U-Net convolutional neural network was implemented in Python using Keras. Predictions were made at the native resolution of the TOF images.

Testing: Performance was evaluated using the Dice Similarity Coefficient (DSC) to compare labeled and predicted classifications on a per voxel basis.

Results

DSCs on the training set were good across all categories, with values of 0.82, 0.89, 0.98, 0.91, 0.88, and 0.99 for arteries, veins, brain, CSF, embolized vessels, and extracerebral tissue, respectively. DSCs on the validation set remained good for arteries, veins, brain, CSF, and extracerebral tissue, with values of 0.72, 0.84, 0.96, 0.90, and 0.97, respectively. Validation DSC for embolized vessels was 0.20.

Conclusions

Automated, deep learning-based vascular segmentation of multi-modal MRI/MRA shows promise for assisting AVM SRS target delineation. Overall, we found good agreement between labeled and predicted vascular maps.
across an anatomically highly diverse dataset. While classification performance for embolized vessels was low compared with other categories, we hypothesize that this is due to the relative rarity of these structures in the training dataset and that performance can be significantly improved with the incorporation of additional training examples.

### Categories

**Physics/technology**

82

### Geographic and Temporal Patterns of Fractionation and Concurrent Chemoradiation for treatment for T2N0M0 Glottic Carcinoma.

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2. 21st Century Oncology, Ft. Myers, FL, USA.
3. 21st Century Oncology, Ft. Lauderdale, FL, USA

#### Purpose

Patients with T2N0M0 glottic carcinoma are subjected to disparate treatment approaches for larynx-preservation with variation in cost, convenience, efficacy and toxicity. We examined geographic and temporal patterns of fractionation and chemoradiation at free-standing radiotherapy centers in the United States.

#### Method

We retrospectively audited fractionation and chemoradiation at 59 centers in 5 geographic regions from 2000-2015. Chi-Squared Test and Fisher’s Exact Tests were used to compare frequencies, Cox proportional hazards model and Kaplan-Meier Procedure were used for survival analyses, and log-rank test to compare survival curves.

#### Results

Among 180 patients, chemoradiation, accelerated-hypofractionation (2.25Gy/fraction), and hyperfractionation was given to 14.4%, 13.3%, and 13.3% respectively. There was striking variation among 5 geographic regions (p<0.001) as well as over time (p<0.001). See Table 1.

#### Table 1.

<table>
<thead>
<tr>
<th>Fractionation by region</th>
<th>Northeast (MA, MD, NJ, NC)</th>
<th>South (AL, NC)</th>
<th>Michigan</th>
<th>Florida</th>
<th>West (NV, WA, AZ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fraction Size</td>
<td>N  %</td>
<td>N  %</td>
<td>N  %</td>
<td>N  %</td>
<td>N  %</td>
</tr>
<tr>
<td>&lt;2Gy.q.d</td>
<td>0  0.0</td>
<td>2  9.5</td>
<td>1  14.3</td>
<td>21  23.6</td>
<td>0  0.0</td>
</tr>
<tr>
<td>&lt;2Gy.q.d</td>
<td>3  7.0</td>
<td>0  0.0</td>
<td>1  14.3</td>
<td>3  3.4</td>
<td>1  8.3</td>
</tr>
<tr>
<td>2.0-2.1Gy.q.d.</td>
<td>32 74.4</td>
<td>12 57.1</td>
<td>5  71.4</td>
<td>60 67.4</td>
<td>7  58.3</td>
</tr>
<tr>
<td>2.25Gy.q.d.</td>
<td>8 18.6</td>
<td>7 33.3</td>
<td>0  0.0</td>
<td>5  5.6</td>
<td>4  33.3</td>
</tr>
</tbody>
</table>

1. Hypofractionation rates varied by geographic location: western/southern-33%, northeast-18.6%, Florida-5.6% and Michigan-0% (p<0.001). Conversely, hyperfractionation rates were Florida-23.6%, Michigan-14%, southern-9.5%, northeast and western-0% (p<0.001). Hypofractionation increased: 6.3% in 2000-2004 to 25.0% in 2010-2015 (p<0.001) and steadily declined for hyperfractionation. Chemoradiation did not vary by region but *increased over time*: 0% in 2000-2004, 17.6% in 2010-2015 (p=.029).

At mean follow-up 32.3months, 36-months-survivals were: accelerated-fractionation-85%, hyperfractionation-81%, and standard-fractionation-66%, (p=0.01); Accelerated-fractionation gave similar 36-months survivals as chemoradiation: 85% and 68% respectively (p=.69) but Chemoradiation worsened acute Grade 2-4 toxicity versus radiotherapy-only: 80.8% and 54.5% respectively (p=0.01, univariate and multivariate).
### Fractionation over time

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 Gyb.i.d</td>
<td>13</td>
<td>40.6</td>
<td>7</td>
<td>10.3</td>
</tr>
<tr>
<td>&lt;2 GYq.d.</td>
<td>1</td>
<td>3.1</td>
<td>3</td>
<td>4.4</td>
</tr>
<tr>
<td>2.0-2.5 Gy q.d.</td>
<td>16</td>
<td>50.0</td>
<td>54</td>
<td>79.4</td>
</tr>
<tr>
<td>2.25 Gyq.d.</td>
<td>2</td>
<td>6.3</td>
<td>4</td>
<td>5.9</td>
</tr>
</tbody>
</table>

### Concurrent chemoradiation over time

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>No Chemotherapy</td>
<td>34</td>
<td>100.0</td>
<td>59</td>
<td>81.9</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>0</td>
<td>0.0</td>
<td>13</td>
<td>18.1</td>
</tr>
</tbody>
</table>

### Concurrent chemoradiation according to cord mobility

<table>
<thead>
<tr>
<th>Cord Mobility</th>
<th>Impaired Cord Mobility</th>
<th>Normal Cord Mobility</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>49</td>
<td>76.6</td>
</tr>
<tr>
<td>%</td>
<td>55</td>
<td>91.7</td>
</tr>
</tbody>
</table>

**Conclusions**

The significant variation of fractionation for glottic T2N0M0 SCC at these 59 centers mirrors the national patterns and trends. We add to the body of evidence supporting use of hypofractionation at 2.25 Gy per
fraction. The data suggests an inferior therapeutic ratio with chemoradiation and should be used only within clinical trials. Guidelines for this group of patients should be more explicit.

Categories
Clinical investigations

OnCare Connect: A text-based platform to allow for earlier interventions to decrease toxicity progression in oncology patients receiving chemoradiation

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Purpose

Patients undergoing combined chemotherapy and radiation therapy experience treatment-related toxicities and commonly have unplanned hospital visits as a result of these toxicities. Such unplanned hospital visits can lead to treatment delays and breaks, possibly compromising oncologic outcomes. A text-based platform, OnCare Connect, was used to target this clinical problem and propose a new approach to help manage cancer treatment-related toxicity.

Method

Fourteen Head & Neck and Lung cancer patients with locally advanced disease receiving concurrent chemoradiation treatment were enrolled onto OnCare Connect. Text messages were delivered using Way to Health, a HIPAA-compliant texting platform. Patients were enrolled onto OnCare Connect during their 6-7 weeks of treatment and had the option of continuing for 1 month after the end of treatment. Patients were texted at least 3 times each week for check-ins and were able to text in from 8am-8pm daily with questions. In this early phase, we explored the feasibility, safety, and acceptability of this novel technology, and used Fisher’s exact test to compare the CTCAEv4.0 toxicity outcomes of these 14 patients with matched control patients treated at our institution.

Results

From April-July 2019, 7 patients with lung cancer and 7 with head and neck cancer treated with concurrent chemoradiation were enrolled onto OnCare Connect. A total of 1,759 text messages were sent and received using Way to Health. OnCare Connect provided medical support 693 times across 867 text messages. The average time to respond to a patient-initiated text message was 3 minutes. A total of 413 treatment-related symptoms were detected by OnCare Connect, of which 64 symptoms were detected prior to provider detection. These symptoms were detected an average of 4.5 days prior to first detection by a provider in clinic. Based on natural language processing, symptoms that were most frequently discussed with patients over text included fatigue, pain, nausea, diarrhea, and anorexia. Compared to 42 matched historical control patients, the 14 patients enrolled on OnCare Connect had fewer CTCAE grade 3+ toxicities (p<0.05). Patient enrolled on OnCare Connect had an average weight loss of 2.9lbs compared to 5.2 lbs. for historical control patients (p=0.12). The use of OnCare Connect resulted in fewer patient calls (p=0.08) and patient portal messages (0.04) during and after treatment completion.

Conclusions

OnCare Connect connected, supported, and strengthened care at our institution. The patient-centered support texting platform that was created was able to detects symptoms earlier and creates pathways to support patients. OnCare Connect was additionally able to extend care capacity for care teams and provide quality and reliable care, resulting in fewer grade 3+ toxicities compared to matched control patients.

Categories
Clinical investigations

Predictors of Pathologic Response after Total Neoadjuvant Therapy (TNT) in Patients with Rectal Adenocarcinoma: A National Cancer Database (NCDB) Analysis

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Purpose

Induction chemotherapy followed by chemoradiation and surgical resection
in rectal cancer, known as total neoadjuvant therapy (TNT), has shown associations with improved pathologic complete response (pCR) rates. We aim to examine the factors associated with pCR and implications of pelvic nodal clearance for the TNT treatment paradigm.

**Method**

We utilized the National Cancer Database to evaluate factors associated with higher pCR rates in locally advanced, non-metastatic rectal cancer patients treated between 2004-2015. Analyses were performed for patients who received either TNT or standard neoadjuvant chemoradiation (non-TNT). Multivariate binomial regression analysis and propensity matching were used to evaluate predictors of pCR. Kaplan-Meier curves and Cox multivariate analysis of survival were performed.

**Results**

Patients were stratified to Non-TNT (n=15,949) and TNT (n=350) groups. Median follow-up was 38m (TNT group) vs 53m (non-TNT group). Propensity matching demonstrated TNT as a significant predictor for pCR (OR 1.54, 95% CI 1.11-2.14, p=0.01). Disease characteristic predictors found to have lower rates of pCR were high grade disease (OR 0.63, p<0.001) and cT4 disease (OR 0.30, p<0.001). Patients achieving pCR demonstrate improved 5-yr OS at 85% (HR 0.34, p<0.001). The 5-yr OS was also improved in the TNT (78%) vs. non-TNT (69%) groups (adjusted HR 0.6, p<0.001).

The TNT group was associated with increased nodal disease burden (OR 3.70, p<0.001), yet complete pelvic nodal clearance rates were higher in the TNT group (OR 1.59, p=0.001). Pooled treatment arms also demonstrate a higher rate of complete nodal response between cN1 disease vs. cN2 disease (65% vs. 57%, respectively, p<0.001). 5-yr OS was improved for those patients who achieved complete pelvic nodal clearance (HR 0.52, p<0.001).

<table>
<thead>
<tr>
<th>Pathologic Response</th>
<th>5-yr OS</th>
<th>HR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT-pN-</td>
<td>85% +/- 3%</td>
<td>0.34</td>
<td>0.28-0.42</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>pT-pN+</td>
<td>77% +/- 12%</td>
<td>0.49</td>
<td>0.30-0.81</td>
<td>p=0.005</td>
</tr>
<tr>
<td>pT+pN-</td>
<td>75% +/- 2%</td>
<td>0.52</td>
<td>0.47-0.58</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>pT+pN+</td>
<td>56% +/- 3%</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
</tbody>
</table>

**Conclusions**

Our findings suggest TNT is correlated with higher rates of pCR and nodal response translating to better survival outcomes. In addition to pCR, pelvic nodal clearance was an independent predictor of increased survival.

**References**


**Categories**

Clinical investigations

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**THURSDAY ORAL**

**16**

**Prediction of toxicity of chimeric antigen receptor T-cell and radiation therapy in patients with relapsed/refractory non-Hodgkin lymphoma**

Christopher Wright, Jonathon Baron, Chibueze Uche, Michael LaRiviere, Ying Xiao, William Arscott, David Miller, Daniel Landsburg, Jakub Svoboda, Sunita Nasta, James Gerson, Elise Chong, Stephen Schuster, Ima Paydar, Amit Maity, John Plastaras

University of Pennsylvania, Philadelphia, PA, USA

**Purpose**

CD19-targeting chimeric antigen receptor (CAR)-T cell therapy has emerged as a promising treatment for relapsed/refractory non-Hodgkin lymphoma (r/rNHL), culminating in 2 FDA-approved therapies, tisagenlecleucel (tis-a-cell) and axicabtagene ciloleucel (axi-cell). However, these therapies can be associated with serious adverse effects, including cytokine release syndrome (CRS) and neurotoxicity. The purpose of this study was to use metabolic tumor volume (MTV) (volume of metabolically active tumor) and total lesion glycolysis (TLG) (MTV times mean standardized uptake volume) to evaluate the association
between baseline tumor burden and adverse effects after CAR-T therapy, as well as to determine the safety of induction-radiation (RT) prior to CAR-T therapy.

Method

Thirty-one patients receiving tisac-cel (n=13) or axi-cel (n=18) between August 2018 and February 2019 for r/rNHL were identified. Patients were divided into three groups based on their timing of RT: a) induction-RT <30d (days) before CAR-T infusion (n=5), b) prior (non-bridging) RT ≥30d (n=7) or c) no prior RT (n=19). RT toxicity was graded by CTCAEv5. CRS and neurotoxicity were graded according to our institutional system and post-CART PET response was determined by the Deauville five-point scale. The study was underpowered to test associations between our predictive factors and outcomes with conventional univariate methods. Random undersampling boost ensemble with tenfold cross-validation univariate analysis was used to test MTV and TLG as predictors for CRS and neurotoxicity.

Results

Median induction-RT dose was 3750cGy (range 2000-4500cGy in 220-400cGy fractions). Grade 1 (G1) and G2 RT-toxicities were observed in 5/5 and 1/5 induction-RT patients, respectively. No G3 or higher toxicities occurred. A complete response on post-infusion PET was observed in 11/26 patients: 3/5 induction-RT, 3/6 prior RT, and 5/15 in no RT.

G3 or higher CRS occurred in no patients in the induction-RT group, 1 patient (14%) in the prior RT group, 4 patients (21%) in the no RT group. Mean MTV was 115mL and TLG was 1201mSUd for induction-RT patients, 135mL and 823SUdMl for prior RT patients, and 54mL and 417SUdMl for no RT patients. MTV (0.86 AUC) and TLG (0.74 AUC) predicted for CRS, but not for neurotoxicity (MTV 0.48 AUC; TLG 0.50 AUC).

Conclusions

Induction-RT prior to CAR-T appears safe in our small sample set. MTV and TLG may predict for CRS following CAR-T cell therapy. No G3 or higher CRS or neurotoxicity was seen in patients who received induction-RT before CAR-T infusion. Future work should be undertaken to validate the hypothesis that initial tumor burden may be used to predict adverse effects from CAR-T cell therapy, and induction-RT may be considered to clinically stabilize patients for bridging and cytoreduction.

Categories

Clinical investigations

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Proton Radiation Therapy for Pediatric Chordomas of the Mobile Spine and Sacrum.

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Daniel W. Kim, MD Thomas F. DeLaney, MD Shannon M. MacDonald, MD PhD Norbert J. Liebsch
Massachusetts General Hospital, Boston, MA, USA

Purpose

Chordomas are rare malignant tumors that arise from remnants of the embryonic notochord. Pediatric chordomas make up 5% of chordoma diagnoses, with the base of skull being the most common site. We report the first cohort of children with spinal and sacrococcygeal chordomas treated with proton radiotherapy (RT).

Method

Thirty-one pediatric patients with chordomas of the mobile spine and sacrum treated with proton (n=7) or combined proton/photon (n=24) RT in our institution between 1988-2018 were retrospectively reviewed. All patients underwent at least one (range, 1 - 6) surgical resection. Four patients were treated with pre- and post-op RT, while 27 patients received only post-op RT. Nine patients received pre-RT chemotherapy. A univariate analysis to identify prognostic factors was performed. Overall survival was calculated using Kaplan-Meier survival analysis.

Results

A total of 17 female and 14 male patients were identified. Median age at diagnosis was 12.3 years (range, 3.6-18.5 y). Twenty-five patients had cervical chordoma, 2 had chordoma of the T-spine, 2 had chordoma of the L-spine and 2 patients had sacrococcygeal chordoma. One patient was initially diagnosed with metastatic disease. The majority of the patients (n=22) were diagnosed with conventional chordoma, 5 with atypical/cellular chordoma, 3 with poorly-differentiated chordoma and 1 had a chordoid subtype. Seventeen patients underwent gross total resection. Eight patients developed progressive disease prior to the delivery of RT. Median total dose was
76 Gy (RBE) [range, 39.7-81.2 Gy (RBE)] delivered in 1.8-2.0-Gy (RBE) daily fractions. The median maximum dose to the spinal cord was 63 Gy (RBE) [range, 30.6-68.5 Gy (RBE)]. Four patients were treated with Pencil Beam Scanning technique, while the remainder were treated with passively scattered proton therapy. At a median follow-up of 7.4 years from the date of diagnosis, progression-free survival (PFS) and overall survival (OS) rates were 62.1% and 65.8% respectively. Ten patients developed recurrences, of which 5 were local, 4 were distant and 1 was iatrogenic. Eight of these patients died of disease. Factors significantly associated with worse survival were: multiple recurrences (HR=10.33, 95% CI 2.95, p<0.001), receipt of pre-RT chemotherapy (HR=5.57, 95% CI 1.30, 23.86, p=0.02) and lower total post-operative RT dose (HR=0.96, 95% CI 0.92, 0.99, p=0.032). Atypical/Cellular subtype was significantly associated with PFS (HR=4.13, 95% CI 1.10, 15.48, p=0.035). Radiation treatment was well tolerated, with most acute side effects limited to mild-to-moderate skin reactions and cervical dysphagia. Two patients developed radiation related late toxicities including 1 case of radiation-induced myelitis and 1 case of Lhermitte’s syndrome. There were no cases of radiation necrosis of the spinal cord.

Conclusions

This is the first report of pediatric spinal and sacrococcygeal chordomas in the literature. PFS and OS rates for pediatric spinal chordomas were found to be similar to their adult counterparts.

Categories

Clinical investigations

Method

A Markov-based cost-effectiveness analysis was constructed to compare the three fractionation schemes above. Transition probabilities for biochemical recurrence (BCR) after initial radiotherapy were taken from HYPO-RT-PC (CF and UHF) and PROFIT (CF and HF), with PROFIT arms (CF and HF) additionally fitted with toxicity survival curves from MDACC data. Upon development of biochemical recurrence, all patients were assumed to receive indefinite androgen deprivation therapy until castration-resistance (transition probabilities from TOAD), after which point docetaxel chemotherapy would be started (transition probabilities from TAX-327). Dosing regimens for CF, HF, and UHF radiotherapy were: 78 Gy in 39 fractions, 60 Gy in 20 fractions, and 40 Gy in 5 fractions, respectively. The analysis utilized a 5-year time horizon, and $100,000 quality-adjusted life year (QALY) willingness-to-pay threshold. Utilities were extracted from the literature; costs were taken from Medicare fee schedules.

Results

At 5 years, total cost was $26.1-26.3K, $21.3K, and $16.1K, with total QALYs of 4.04-4.08, 4.01, and 4.07 for CF (PROFIT/HYPO-RT-PC), HF (PROFIT), and UHF (HYPO-RT-PC) therapies, respectively. Compared to UHF regimens, both CF regimens (ICER: $906K/QALY and $400K/QALY) and HF regimen (ICER: -$86K/QALY) were not cost-effective. For validation of UHF cost and effectiveness, additional analysis was run from a pooled, multi-institutional cohort of 957 intermediate-risk patients4, yielding similar results (cost of $15.3K and effectiveness of 4.06 QALYs at 5 years) as from HYPO-RT-PC. When comparing
CF directly with HF, utilizing PROFIT/MDACC data only, CF was not cost-effective compared to HF (ICER: $149K/QALY).

Conclusions

At 5 years, UHF radiotherapy is found to be cost-effective compared to both CF and HF radiotherapy regimens. Additional long-term follow-up is needed in UHF at later time points to evaluate the robustness of this result beyond 5 years.

References


Categories

Socioeconomic/ethical issues/health outcomes research

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Updated Completion Rate and Timing of Surgical Resection for Retroperitoneal Sarcomas Managed with Hypo-Fractionation

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Purpose

Retroperitoneal sarcomas (RPS) are difficult to resect with wide margins, likely contributing to their high local recurrence rates. Current management in large or intermediate/high grade tumors includes neoadjuvant radiotherapy (RT). Conventional RT is delivered with treatment Monday – Friday over 5-6 weeks. Hypofractionated RT (hypo-RT) may be a more efficient alternative, shortening the treatment period and potentially increasing the potency of radiation. This study updates our experience of RT of retroperitoneal tumors for feasibility and tolerability of planned therapy and surgical resection.

Method

An IRB-approved institutional retrospective study was conducted with patients treated between 01/2017 to 10/2019. Bone sarcomas, cardiac sarcomas, gastrointestinal stromal tumors, Kaposi’s sarcomas, rhabdomyosarcoma, and uterine carcinosarcomas were excluded. Thereafter, we identified the records of 44 patients (58 sites) with retroperitoneal or pelvis/trunk sarcomas, treated with no neoadjuvant RT, neoadjuvant standard RT (44Gy – 57.5Gy total dose in 25 – 28 fractions), or neoadjuvant hypo-RT (20Gy – 39Gy total dose in 5 – 13 fractions). Thirty-five of these patients were treated with RT to a primary or recurrent tumor for aggressive local control with or without intended surgical resection. Fifteen patients (42.9%) were managed with surgical resection of the treated tumor after neoadjuvant RT. An additional 1 patient is planned for prospective surgical resection.

Results

At an average follow-up time of 13.82 months (0.33 – 29.14mos) from the start of RT, 19 (54.3%) patients were managed with standard RT and 16 (45.7%) patients with hypo-RT. The median total RT dose for standard RT was 50Gy at 2Gy per fraction in 25 fractions. The median total RT dose for hypo-RT was 25Gy at 5Gy per fraction in 5 fractions. The majority of patients in the standard RT arm had completed planned radiation (94.7%) with 1 residual patient completing RT currently with a planned resection. All patients (100%) in the hypo-fx completed planned RT. All patients having undergone surgical resection were resected within 3 months after completion of RT. The median time to surgical resection from the start of treatment in the standard RT arm was 3.19 mos (2.14 – 3.98mos) and in the
hypo-RT arm 1.00mos (0.46 – 1.91mos).

Conclusions
We found both hypofractionated and standard RT to be well tolerated. Although the number of patients is low in our current study, we found the median time interval from the start of RT to planned surgical resection to be more than 2 months less in the hypo-RT compared with standard RT arm. All patients in the hypo-RT arm successfully completed neoadjuvant RT. Further research is needed to identify biological alterations to tumor cells and surrounding stroma that characterize the effects of hypofractionation, and which might be further potentiated for optimal tumor control.

Categories
Clinical investigations

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Development and Validation of a Novel TP53 Mutation Signature as a Novel Subclass Associated with Poor Prognosis in Primary Prostate Cancer.

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Purpose
TP53 gene mutations have been linked to inferior outcomes in prostate cancer. We sought to develop an RNA-based genomic signature to predict underlying TP53 gene mutations.

Method
Using genomic expression profiles from The Cancer Genome Atlas (TCGA), we developed a mutation signature score and validated it in three retrospective and one prospective cohort. Area under the receiver operating characteristic (ROC) curve assessed model accuracy in predicting TP53 mutations, and Cox regression models measured association between the signature and progression-free survival (PFS) and metastasis-free survival (MFS).

Results
The TP53 signature score achieved an AUC of 0.84 in the training cohort and 0.82 in the validation cohort. In model training, a high TP53 signature score was associated with worse 3-year PFS (64% vs 83%, p < 0.0001). In three retrospective cohorts, a high score was similarly prognostic for poor 5-year MFS: 46% vs 81% (HR:3.05, p < 0.0001, JHU cohort), 64 % vs 83% (HR:2.77, p<0.0001, Mayo cohort), and 71% vs 97% (HR:6.8, p=0.0001, BWH cohort). In TP53-wildtype tumors, a high signature score was also associated with worse 5-year MFS (50% vs 82%, HR 3.05, p < 0.0001). The signature score remained prognostic on multivariable analysis and in a subgroup of radiation-managed patients.

Conclusions
This novel mutational signature predicted for the presence of aTP53 gene mutation and was independently associated with poor MFS, even in TP53-wild type tumors. Results suggest increased sensitivity in detecting TP53 mutations compared to immunohistochemical assays. This signature can be used to strengthen existing clinical risk stratification tools.

References

Categories
Translational science