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COVID-19 Impacts on Medical Education

Campbell et al

In this month’s Oncology Scan, the Education editors conduct a sophisticated, instructive review of the impacts of COVID-19 on medical education. In the process they provide multiple frameworks that can be applied to raise the quality of medical educational research. First they summarize findings of a “rapid,” large-scale systematic review of medical education interventions related to the pandemic. Specific recommendations for radiation oncology include higher-level evaluations of online learning approaches and virtual continuing medical education. Pandemic effects on faculty development, and learner/faculty well-being. Comprehensive evaluation should include not just learners’ reactions or satisfaction with learning, but further impacts such as changes in attitudes, knowledge, or skills, changes in behaviors, and changes in organizational practices or clinical outcomes.

The editors review recent research on e-learning in the workplace and contouring courses applying these standards. Finally, they describe COVID-19-era adaptations of residency programs to ensure safety and assess well-being of residents.

Virtual Radiation Oncology Peer Review and Decreased Engagement

Hughes et al

These authors studied prospectively whether virtual rather than in-person meetings affected the efficacy and engagement of peer review. The department transitioned peer review to virtual meetings in March 2020 during the COVID-19 pandemic. Among a total of 3,372 radiation plans, deviations were identified in 2.5% of cases reviewed virtually compared with 7.3% reviewed in-person, and in the virtual group, 90.3% of cases had no discussion versus 72.8% in the in-person group. Discussions of specific topics were decreased but among cases that were discussed, the rate of identified deviations was similar virtually or in-person. The authors conclude that virtual peer review is associated with a decline in identified deviations and less discussion, and they hypothesize that decreased engagement (based on amount of discussion) resulted in identifying fewer deviations.

ASTRO’s Framework for Radiopharmaceutical Therapy Curriculum Development

Kiess et al

In 2017, the ASTRO Radiopharmaceutical Therapy (RPT) Workgroup was formed and now offers a framework for RPT curriculum development. The purpose is to integrate this modality into radiation oncology resident education. The framework describes the core RPT knowledge required to select patients, prescribe, safely administer, and manage related adverse events. Then, it defines the most important topics for preparing residents for clinical RPT planning and delivery. This document was approved by the ASTRO Board of Directors in the Fall of 2021. The authors intend for this to stimulate training and educational programs in support of RPT practice development.

Chemoradiation with Hypofractionated Proton Therapy in Non-Small Cell Lung Cancer

Hoppe et al

Proton therapy may allow for safe delivery of hypofractionated radiotherapy for non-small cell lung cancer (NSCLC). These authors report a phase I-II single-arm multicenter trial. Patients had AJCCv7 stage II-III unresectable NSCLC and received hypofractionated proton therapy at 2.5–4 Gy per fraction to a total dose of 60 Gy, with concurrent doublet chemotherapy. The primary endpoint was overall survival at 1 year. Among 28 evaluable patients, the median age was 70 years; patients were predominantly male (N=20), white (N=23), and prior smokers (N=27). Most had stage III NSCLC (N=22). At a median follow-up of 31 months, the 1- and 3-year overall survival rates were 89% and 49%, and progression-free survival rates were 58% and 32%. 14% of patients had grade 3 or higher pulmonary toxicity and there was no grade 3 esophagitis. An accompanying editorial by Brownstein and Salama contextualizes this and the following article within the landscape of locally advanced lung cancer research where hypofractionation remains controversial.

Hypofractionated Proton Therapy and Chemotherapy for Non-Small Cell Lung Cancer

Contreras et al

This phase I trial evaluated the maximum tolerated dose (MTD) of hypofractionated proton beam radiation therapy with concurrent weekly carboplatin/paclitaxel in patients with stage II-III non-small cell lung cancer. The trial used Time to Event–Continuous Reassessment Method. MTD was defined as the dose associated with a 20% probability of protocol-specified serious adverse events (SAEs). Among 20 evaluable patients, the median age was 66.5 years; the majority (60%) were male, had squamous cell carcinoma (70%) and stage III A (75%). Dose assignments were 52.5 Gy (n=2), 56.25 Gy (n=4), and 60 Gy (n=14) in 15 fractions. 7 patients (35%) had grade 2 esophagitis and 1 patient (5%) had grade 2 pneumonitis at a median follow-up of 20.3 months.
there were no grade 4 or 5 SAEs, though there were three additional SAEs outside of the acute toxicity window. The 2-year overall survival, and local, regional, and distant control rates were 48%, 84%, 77%, and 79%. The authors conclude that the schedule of 60 Gy in 15 fractions was tolerated and effective, although late SAEs emerged.

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**Prognostic Role of PD-L1 Expression in Stage III Non-Small Cell Lung Cancer**

*Bryant et al*

These authors measured pre-treatment tumor PD-L1 expression in 312 veteran patients with stage III NSCLC treated with definitive chemoradiation and adjuvant durvalumab. Progression-free survival (PFS) and overall survival (OS) were estimated in PD-L1 expression subgroups. PD-L1 expression was <1%, 1-49%, and 50-100% in 34.9%, 30.7%, and 34.3% of patients, respectively. Increasing PD-L1 expression was associated with longer PFS and OS. Compared to the no-durvalumab group, PFS was longer for PD-L1 50-100% and PD-L1 1-49% among those receiving durvalumab but not for PD-L1 <1%. Similar results were found for OS, with no significant difference between the no-durvalumab group and the PD-L1 <1% group. The authors conclude that at least in this studied population, patients with PDL1 expression <1% may have limited benefit from adjuvant durvalumab.

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**A Secondary Analysis of Nodal Metastasis in NRG/RTOG 9501, NRG/RTOG 0234, and EORTC 22931**

*Lu et al*

These authors present a secondary analysis of three prospective randomized trials from RTOG/NRG Oncology and the European Organisation for Research and Treatment of Cancer. Their aim was to study the relationships between the number of pathologically positive lymph nodes (LN) and recurrence and mortality. 947 head and neck cancer patients had surgery and post-operative radiation +/- systemic therapy. In multivariable analyses, disease-free and overall survival decreased with each LN. Locoregional recurrence risk increased up to 5 LNs but then plateaued, whereas distant metastasis risk increased continuously with increasing LN. These findings reinforce the importance of the number of LN in determining the prognosis of surgically resected head and neck cancer.

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**Phase 2 Study of Apatinib in Radiation-Induced Brain Injury among Head and Neck Cancer Patients**

*He et al*

Apatinib is an oral tyrosine kinase inhibitor that selectively inhibits vascular endothelial growth factor receptor 2. These authors from Sun Yat-sen Memorial Hospital in China aimed to assess the safety and efficacy of apatinib to treat radiation-induced brain injury in a phase 2 single-arm study. The apatinib dosage was 250 mg daily orally for 4 weeks. The primary outcome was the proportion of patients with ≥25% reduction in baseline brain edema volume on magnetic resonance fluid attenuated inversion recovery imaging at week 4. Of the 36 patients enrolled and evaluable, 22 achieved the primary endpoint. The most common grade 1-2 adverse events were hand-foot syndrome, fatigue and hypertension. There were no treatment-related grade 4-5 toxicities. The authors propose that oral apatinib is well-tolerated and shows promising efficacy for radiation-induced brain injury.

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**Retreatment of Recurrent or Second Primary Head and Neck Cancer After Prior Radiation**

*Ward et al*

This is an executive summary of the American Radium Society Appropriate Use Criteria recommendations for reirradiation for recurrent or second primary head and neck cancers. These were based on a structured literature search and anonymized voting process conducted via the modified Delphi method. The areas covered included patient selection, adjuvant reirradiation, definitive reirradiation, stereotactic body radiation, and reirradiation of non-squamous cancer. This comprehensive summary provides an up-to-date clinical review as well as a basis for future research.

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pN0(i+) and pN1mi Breast Cancer in the Modern Era
Dosani et al

These authors compared locoregional relapse-free survival (LRRFS) in patients with pN0(i+) and pN1mi relative to pN0 and pN1a disease. From their institutional database, they identified 10,271 patients referred between 2006-2011 with newly diagnosed pT1-T2; pN0, pN0(i+), pN1mi, or pN1a breast cancer. The median follow-up was 9.3 years. Locoregional radiation (LRRT) was increasingly given to patients with increasing pathologic stage. In pN0 (n=7,492), pN0(i+) (n=305), pN1mi (n=619) and pN1a (n=1,855) disease, LRRT was used in 1.1%, 24.3%, 45.7% and 71.1%. Outcomes were not significantly different among the groups, with LRRFS of 96%, 92%, 97%, and 96% (p<0.001). On multivariable analysis, systemic therapy was associated with improved LRRFS in pN0(i+) patients and pN1mi patients. The authors conclude that with modern surgery, systemic therapy, and locoregional radiation, patients with pN0(i+) and pN1mi had 10-year locoregional recurrence risks ≤10% after either breast conserving surgery or mastectomy. LRRT contributed to a trend towards increased LRRFS in pN1mi but not in pN0(i+) disease.

Outcome of Patients with Testicular Seminoma who Relapse after Adjuvant or Curative Radiotherapy
Terbuch et al

This report examined patients with clinical stage I or II testicular seminoma who had orchectomy and radiotherapy and then relapsed. 61 patients from 17 centers in 11 countries were identified. The median time to relapse after radiotherapy was 15.6 months but 36% of patients relapsed more than 2 years after radiotherapy and 11.5% relapsed more than 5 years after radiotherapy. One third of relapses was detected due to patients' symptoms and two thirds were detected during routine follow-up. 93% of cases were treated with cisplatin-based chemotherapy. At a median follow-up of 9.9 years after relapse, the 5-year disease-free survival was 90% and the 5-year overall survival was 98%. Only one patient died due to disease progression. The authors conclude that cisplatin-based chemotherapy for seminoma patients who have relapsed after treatment with radiotherapy produced excellent rates of salvage.

Antibiotic-Induced Gut Microbiota Depletion Accelerates Recovery of Radiation-Induced Oral Mucositis in Rats
Al-Qadami et al

This study explored the role of the gut microbiota in the pathogenesis of radiation-induced oral mucositis in rats. Male rats were treated with 20 Gy radiation to the snout, with or without antibiotic-induced microbiota depletion (AIMD). Mucositis severity was assessed, and tongue tissues were collected on days 9 and 15 post-ration. The rats that had AIMD had significantly shorter duration of severe mucositis. Macroscopically, the tongue ulcer-like area was smaller and microscopically, a smaller percentage of the mucosal ulcer was observed in the dorsal tongue in AIMD treated rats. There were lower levels of IL-6, IL-1β, and TLR4 in their tongue tissues. The authors conclude that gut microbiota affect oral mucositis pathogenesis, and microbiota-targeted interventions may improve recovery.

68Ga-DOTATATE PET-based Radiation Contouring for Meningioma Patients
Perlow et al

These authors hypothesized that in meningioma patients, 68 Ga-DOTATATE PET scan-based treatment planning would enable contouring of smaller radiation volumes and detect additional areas of disease compared to standard MRI alone. 4 specialized radiation oncologists and 3 neuroradiologists anonymously and non-sequentially contoured 25 de-identified meningioma patients who received both a 68 Ga-DOTATATE PET and an MRI for radiation treatment planning. Median PET volumes were smaller (2.09-8.36 cc) then median MRI volumes (16.94-25.53 cc). 7/25 (28%) patients had new nonadjacent areas contoured on PET by at least 6 of the 7 physicians that were not contoured by these same physicians on the MRI. The authors conclude...
that 68 Ga-DOTATATE PET imaging helps draw more precise volumes and finds undetected areas of disease not seen on MRI. Editorials by Beavis and Prasad et al. provide historical, practical, and research context for the application of this novel imaging.

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**A Predictive Biophysical Model of the Combined Action of Radiotherapy and Immunotherapy in Cancer**

**Friedrich et al**

The authors present a biophysical model predicting the combined interaction of radiotherapy and immunotherapy in cancer. This model considered the dependences of primary and distal tumor masses, immune cell kinetics targeting tumor cells, and signals causing immune cell replenishment after radiation mechanistic interpretation of the low frequency of abscopal responses. The model allowed a quantitative mechanistic interpretation of the interaction of radiation with checkpoint blockade.

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— Sue S. Yom, MD, PhD, FASTRO, Editor-in-Chief

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