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10-1-2020

American Radium Society (ARS) and American College of Radiology (ACR) Appropriate Use Criteria Systematic Review and Guidelines on Reirradiation for Non-small Cell Lung Cancer (NSCLC)

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Recommended Citation

Simone C, Amini A, Chetty I, Choi JI, Chun S, Donington J, Edelman M, Higgins K, Kestin L, Mohindra P, Movsas B, Rodrigues G, Rosenzweig K, Rybkin I, Shepherd A, Slotman B, Wolf A, and Chang J. American Radium Society (ARS) and American College of Radiology (ACR) Appropriate Use Criteria Systematic Review and Guidelines on Reirradiation for Non-small Cell Lung Cancer (NSCLC). *International Journal of Radiation Oncology Biology Physics* 2020; 108(2):E48-E49.

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Background: Racial differences in clinical outcomes among laryngeal cancer patients have been reported and Black American patients appear to have worse survival compared to White Americans. However, there are not many studies looking at the potential racial differences in outcomes in T1 Glottic cancers. One of the hypotheses underlying racial differences in clinical outcomes is lack of adequate access to healthcare for the Blacks. Thus, the Blacks may present with more advanced stages at the time of diagnosis, thus leading to poorer outcomes. We hypothesized that since T1 glottic cancer is one of the earliest stages, with the least tumor burden, outcomes should be similar between the two races. At our institution, a safety-net academic medical center, there are no differences in the treatment being given Blacks or Whites, stage-for-stage. To our surprise, we found poorer clinical outcomes for the blacks. What we report here is a hypothesis generating analysis.

Objectives: To evaluate the impact of race (Black vs. White) on the outcome of T1 glottic squamous cell carcinoma (SCCa) in patients treated with radiation therapy (RT) alone.

Methods: Between 2002 and 2018, twenty-five (37.3%) Black patients and forty-two (62.7%) White patients with T1 glottic SCCa underwent RT in our academic state institution. Chi-square test, Kaplan-Meier method, and Cox regression models were used to assess for racial influence; p-values less than 0.05 were considered statistically significant. The SPSS 24.0 software was used for data analyses.

Results: The baseline characteristics of all 67 T1 glottic SCCa patients documented. The median follow-up duration was 51 months (range, 0-266 months). Black patients (n=14; 20.9%) and White patients (n=28; 41.8%) were treated with a conventional schedule (CONV) 2 Gy/ day; total dose 66 Gy/ 7 weeks. Eleven Black patients (16.4%) and White patients (n=14; 20.9%) were treated in a hypo-fractionated (HYPO) schedule 2.25 Gy/ day; total dose 63 Gy/5 weeks. The 5-year overall survival (OS) for Blacks vs. Whites treated with CONV was 51.6 vs. 66.0% (p= 0.001). For those treated with HYPO, the OS was 85.7 vs. 99.6% (p= 0.001). The 5-year local relapse free survival (LRFS) for Blacks vs. Whites treated with CONV was 34.1 vs. 40.9% (p= 0.163) and for those treated with HYPO was 42.6 vs. 72.7% (p= 0.163), showing no statistical significance between the two groups. In the univariate Cox regression analysis, the covariates of ethnicity, RT type, voice-hoarseness, gender, and type of insurance were statistically significant with p-value less than 0.05. However, in the multivariate Cox regression analysis only, the co-variables of ethnicity-Black (HR, 4.39; 95% CI, 1.46-13.17; p=0.008), RT type-CONV (HR, 20.82; 95% CI, 3.63-119.32; p=0.001), voice-hoarseness (HR, 3.80; 95% CI, 1.26-11.41; p=0.017), and gender-male (HR, 7.08; 95% CI, 1.46-34.22; p=0.015) were statistically significant.

Conclusions: Race appears to be an independent prognostic factor for OS in T1 glottic cancers. Although local control rates were poorer for Blacks, it didn't reach statistical significance.

P065

American Radium Society® (ARS) Appropriate Use Criteria on Radiation Therapy in Oligometastatic or Oligoprogressive Non-Small Cell Lung Cancer (NSCLC)



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Background: Recently, small randomized phase II studies have demonstrated significant improvements in progression free survival (PFS) and overall survival (OS) with the addition of stereotactic body radiation therapy (SBRT) in stage IV non-small cell lung cancer (NSCLC) patients with oligometastatic disease. Yet, current guidelines on local therapy for oligometastatic disease are lacking.

Objectives: The American Radium Society (ARS) Appropriate Use Criteria Thoracic Panel was assigned to create guidelines on consolidative local therapy (radiotherapy, surgery, and others) recommendations for oligometastatic and oligoprogressive NSCLC patients.

Methods: A panel of radiation, medical, and surgical oncologists at academic and private practices evaluated best practice based on the current available data on the following topics/scenarios: 1) defining oligometastasis and oligoprogression, 2) role of radiation in oligometastatic disease in the up-front setting, 3) role of consolidative radiation after stable/partial response following upfront systemic therapy, 4) management of the primary and N1-N3 nodal disease, 5) role of consolidative radiation for oligoprogression during systemic therapy, 6) role of consolidative radiation for cases with targetable driver mutations, and 7) management of brain metastases in the oligometastatic or oligoprogressive setting.

Results: Based on current data and consensus by the expert panel, the optimal definition of oligometastatic and oligoprogression is ≤ 3 metastatic deposits, not including the primary tumor, with the understanding that ongoing trials may alter this threshold. In the scenario of radiation for oligometastatic disease in the up-front setting, several single-arm prospective trials support this approach and, therefore, this may be one feasible approach, although most contemporary randomized studies along with ongoing phase III trials are designed with standard of care systemic therapy in the upfront setting, followed by locally ablative therapy (LAT). Two randomized controlled phase 2 studies have demonstrated that the addition of local consolidative RT or surgery for oligometastatic NSCLC improved PFS and OS. Therefore, the panel supports the utilization of LAT as an option following upfront systemic therapy in oligometastatic patients. Thoracic nodal treatment is also discussed with various radiation approaches, including hypofractionation and SBRT. Prospective data on SBRT for oligoprogression are limited, but there is some suggestion that LAT may be beneficial in select patients. In patients with targetable mutations, a similar approach should be offered, although the consensus panel acknowledges a low sample size of these patients in existing trials. Lastly, the treatment of brain metastases should be based on multiple factors including the number of metastases, patient symptoms, and presence of a molecular target.

Conclusions: The guideline topics discussed here are the first in the management of oligometastatic and oligoprogressive NSCLC based on a multidisciplinary panel of physicians. Finalized recommendations from the committee will be presented at the annual ARS meeting.

P066

American Radium Society (ARS) and American College of Radiology (ACR) Appropriate Use Criteria Systematic Review and Guidelines on Reirradiation for Non-small Cell Lung Cancer (NSCLC)



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Background: Reirradiation (reRT) for locoregional recurrences can provide durable control and improved symptoms and progression-free survival for select NSCLC patients. Thoracic reRT, however, is particularly challenging due to its considerable risk and the current lack of standardized approaches, guidelines and dose constraints. To date, no systematic review on the safety and efficacy of reRT for NSCLC exists, and no dedicated guidelines are available.

Objectives: This ARS-ACR Appropriate Use Criteria Systematic Review and Guidelines on Reirradiation for NSCLC provides direct guidance on the safety and efficacy of reRT and recommends consensus dose constraints for thoracic reRT to minimize risks of high grade toxicities.

Methods: A PRISMA systematic review assessed all studies published through 3/2019 evaluating toxicities, local control and/or overall survival for NSCLC thoracic reRT. Of 236 articles, 49 remained after exclusions (3 prospective) and formed the basis for these recommendations on: 1) the role of concurrent chemotherapy with reRT, 2) factors associated with toxicity from reRT and 3) what reRT modalities, dose-fractionation schemas and dose rates should be used. Composite dose constraints were also recommended.

Results: The available data suggest potential benefit in clinical outcomes with concurrent chemoradiation for reRT, but the decision should be based on patient performance status, tolerance to prior systemic therapy and other individual patient/tumor characteristics. There are no data to guide the use of concurrent targeted therapy or immunotherapy with reRT, and this is not recommended outside of a clinical trial. Acute esophagitis and pneumonitis and late pulmonary, cardiac/great vessel, esophageal, brachial plexus and spinal toxicities are dose limiting for reRT. Limited data exist regarding the use of hyperfractionation and low- or high-dose rate reRT for NSCLC. For conventionally fractionated reRT, intensity-modulated radiation therapy (IMRT) is recommended over 3D conformal radiation therapy (3DCRT) to increase dose conformality. Particle therapy may further reduce toxicities and/or enable safer reRT dose escalation compared with 3DCRT and IMRT. Stereotactic body radiation therapy (SBRT) can provide increased conformality and dose escalation and is optimal for primary-alone failures, but caution is needed for central reRT with SBRT. Recommended reRT composite dose constraints in 2 Gy equivalent dose are: esophagus V60 <40% and DMax <100-110 Gy, lung V20 <40%, heart V40 <50%, aorta/great vessels DMax <120 Gy, trachea and proximal bronchial tree DMax <110 Gy, spinal cord DMax <57 Gy, and brachial plexus DMax <85 Gy.

Conclusions: For the first time, consensus dose constraints for thoracic reRT are recommended to minimize the risks of high-grade and potentially fatal toxicities from repeat radiotherapy. Additional prospective data are needed, and toxicities should be correlated with reRT course and composite dose constraints.

P067

Gamma Knife Boost for Head and Neck Cancers with Skull Base Extension: A Case Series



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Background: Many Head and Neck Cancers (HNC) have a predilection for perineural spread which can track proximally and lead to skull base involvement. In cases of skull base involvement, including gross/residual

disease after surgery, it can be challenging to deliver tumoricidal radiotherapy dose without exceeding nearby critical structure constraints despite the adoption of highly conformal approaches such as IMRT and proton. The use of GammaKnife stereotactic radiosurgery as a boost (GK-boost) to IMRT may further improve sparing of these critical structures while escalating dose to disease in the skull base.

Objectives: In this case series we report the clinical outcomes of patients receiving a GK-boost to the skull base as a component of their overall IMRT plan.

Methods: Patients with HNC and gross/residual skull base disease after surgery treated with conventionally fractionated radiation therapy (IMRT/IMPT) plus a GK-boost between March 2014 and September 2019 were retrospectively reviewed. Five patients had squamous cell carcinomas (SCC) from a skin primary, one patient had a SCC of the oral cavity, and one patient had an adenoid cystic carcinoma. Treatment toxicity, survival, and local control were evaluated.

Results: Of the patients evaluated, 4 received adjuvant radiotherapy after surgery and 3 were treated with definitive radiotherapy. The median dose for IMRT was 66 Gy in 30-33 Fx. The median GK-boost dose was 8-11 Gy in a single fraction. The majority of patients received the GK boost after a median interval of 9 days post IMRT. The boost was delivered to the trigeminal nerve tract in five patients and the facial nerve tract in two patients. Median follow-up was 33 months. There were no local failures. There was 1 death and 1 regional recurrence in the same patient. This patient had a regional recurrence 11.2 months after completing treatment in the left orbit outside the prescribed PTV, which received 30 Gy or less. There were no G3 or higher acute toxicity associated with GK boost. There were 2 patients that developed asymptomatic temporal lobe radionecrosis.

Conclusions: GammaKnife boost to the skull base is well tolerated and provides a durable local control benefit. An ongoing dosimetric comparative study will assess the extent of normal tissue dose sparing. A larger prospective study is needed to validate these clinical findings.

P068

Radiomics Analysis and Unsupervised Self-Organizing-Map Technique to Predict Radiation-Induced Pneumonitis in Patients with Lung Cancer



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Background: Lung radiation pneumonitis (RP) is one of the major toxicities experienced by lung cancer patients (13%–37%) receiving thoracic radiation therapy (RT) (Kocak Z, et al. Int. J. Radiat. Oncol. Biol. Phys. 2005 and Rodrigues G, et al. Oncol. 2004). Investigation of imaging biomarkers that can predict the incidence of RP can be useful toward reduce the probability of RP development. In this pilot study, we investigated the application of Kohonen Self-Organizing Map (K-SOM; a type of adaptive model that is trained using unsupervised competitive-learning (Kohonen T, Springer 1995)), for analysis of radiomic features extracted from normal lung tissue of non-RP and RP patients. The goal was to build an adaptive model to stratify patients and to reveal dominant characteristics of radiomics features for patient stratification. These characteristics are likely to remain unnoticed using conventional statistical analysis.

Objectives: To perform deep and unsupervised analysis of radiomics features extracted from planning CT images of normal lung tissue for patients with locally advanced, non-small cell lung cancers (NSCLC) to characterize and stratify patients with and without radiation-induced RP.

Methods: Planning CT images of 41 patients (14 with RP and 27 with no evidence of RP) with stage-III lung cancers, treated with IMRT/3D-CRT, were studied. One hundred sixty eight radiomics features were extracted from the volume of normal lung tissue receiving ≥ 20 Gy, excluding the