

Year in Review: The studies that changed the oncology practice in 2018: focus on radiation therapy

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YEAR IN REVIEW: THE STUDIES THAT CHANGED THE ONCOLOGY PRACTICE IN 2018: FOCUS ON RADIATION THERAPY

The year of 2018 was a very important year for oncology. Numerous groundbreaking studies and novel approaches were published and or presented. For instance, the seminal work on the discovery of cancer therapy by inhibition of negative immune regulation was especially important and granted the 2018 Nobel Prize in Physiology or Medicine. Within the radiation therapy arena the importance of ablative treatment for oligometastatic patients has the ability to start a revolution on how we treat stage IV cancers⁽¹⁾.

The current article aims to review the most relevant studies exploring radiation therapy (RT) as main intervention published or presented in 2018. We performed a configuring review aiming to unravel and understand the RT based changed practice published or presented articles. It is important to note that configuring reviews have the different purpose of aiming to find most important cases and so are not necessarily attempting to be exhaustive in their searching.

2018 GROUNDBREAKING RADIATION THERAPY BASED STUDIES PER SITE

GASTROINTESTINAL

Oesophagus NEOCRTEC5010 – Role of chemoradiation

In the open-label phase III randomized clinical trial (RCT), 451 patients with potentially resectable thoracic oesophageal disease clinically staged T1-4, N1, M0 or T4, N0, M0 were randomized to receive neoadjuvant chemoradiation (CRT) - vinorelbine and cisplatin / 40 Gy in 20 fractions - followed by esophagectomy (n = 224) or surgery alone (n = 227). The pathologic complete response (CR) rate was 43.2% in the CRT group. Compared with the group that underwent surgery alone, the CRT patients had a higher R0 resection rate (98.4% vs 91.2%; p=0.002), a longer median overall survival (OS) (100.1 months vs 66.5 months; p=0.025), and prolonged disease-free survival (PFS) (100.1 months vs 41.7 months; p<0.001)⁽²⁾.

Liver – Sorafenib versus transarterial chemoembolization plus RT

In a RCT of 90 treatment-naive patients with liver-confined hepatocellular carcinoma with macroscopic vascular invasion were randomly assigned to receive sorafenib or transarterial chemoembolization (TACE) plus RT (45 Gy with the fraction size of 2.5 to 3 Gy). The 12-weeks PFS rate was significantly higher in the TACE-RT group than the sorafenib group (86.7% vs 34.3%; p < 0.001). The TACE-RT group showed higher radiologic response rate at 24 weeks (15 [33.3%] vs 1 [2.2%]; p<0.001), longer median time to progression (31.0 vs 11.7 weeks; p < 0.001) and longer OS (55.0 vs 43.0 weeks; p = 0.04)⁽³⁾.

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PROSTATE

SPORTT Trial RTOG 0534 – importance of treatment selection

In the NRG (former RTOG) 0534 SPPORT trial 1,792 patients were randomly placed into three treatment groups: prostate bed radiation therapy (PBRT) alone, PBRT plus short-term androgen deprivation therapy (STAD), and PBRT plus pelvic lymph node radiotherapy (PLNRT) plus STAD (trimodality group). At 5 years, freedom-from-progression (FFP) was 89.1% in trimodality therapy for patients with persistent or rising PSA levels after prostatectomy compared to 82.7% with PBRT plus STAD and 71.7% with PBRT alone ($p < 0.0001$)⁽⁴⁾.

STAMPEDE H ARM – focal therapy and metastatic disease

According to results from a pre planned analysis of the STAMPEDE trial⁽⁵⁾ RT to the prostate improved OS in men with newly diagnosed metastatic prostate cancer and who presented low metastatic disease burden, but not in those with higher burden of disease. The study included 2,061 patients and randomly allocated them to standard of care (SOC) treatment (androgen deprivation therapy plus early docetaxel) or SOC plus RT to the prostate (55 Gy/20 fractions daily over 4 weeks or 36 Gy/6 fractions weekly over 6 weeks).

At 3 years, OS was 65% for patients receiving RT and 62% for men in the control arm. Significant improvement in OS was seen in the subgroup of men with low metastatic disease burden (HR, 0.68; $p = 0.007$).

HYPO-RT-PC Trial – feasibility of ultra-fractionated RT

Radiation therapy given in high doses over a shorter period of time is safe and effective for patients with prostate cancer, according to a RCT trial presented at ESTRO-37⁽⁶⁾. This first RCT with ultra-fractionated RT randomized 1,200 patients to receive standard RT in 39 fractions of 2Gy (8 weeks) or 7 fractions of 6.1Gy in 3.5 weeks. At 5 years follow-up time point, the local control and toxicities rates were similar in both groups.

GYNECOLOGIC CANCER

PORTEC 3 – RT plus or minus adjuvant chemotherapy for high-risk endometrial cancer

For patients with high-risk endometrial cancer the RCT (PORTEC 3) results showed no benefit on the addition of chemotherapy to adjuvant RT⁽⁷⁾. In the PORTEC 3 RCT patients with stage I-III serous and clear cell histology, stage I endometrioid-type grade 3 with deep myometrial invasion or lymph-vascular space invasion (or both) or endometrioid-type stage II-III, were randomized after surgery to receive chemoradiation (chemoRT) versus RT alone. There was no difference in 5-years OS rates between the groups (81.8% chemoRT versus 76.7% RT; $p = 0.11$). Five years failure-free survival showed benefit for the chemoRT (75.5% versus 68.6%; $p = 0.022$), although it was associated with an important increase in grade 3 or worst toxicity events (60% versus 12%; $p < 0.05$).

HEMATOLOGICAL CANCER

International Lymphoma Radiation Oncology Group – importance of standard approach

The International Lymphoma Radiation Oncology Group (ILROG) published in 2018 a new guideline for total body irradiation (TBI)⁽⁸⁾. Total body irradiation is an important part of treatment for patients with hematological diseases, such as acute lymphoid leukemia (ALL) or acute myeloid leukemia (AML), as a part of conditioning regimen for hematopoietic stem cell transplantation, since it allows not only immunosuppression to prevent rejection of donor hematopoietic cells, but also aims to eradicate malignant cells. There are also advantages of TBI in comparison to chemotherapy regimens for myeloablation, such as achieving sanctuaries (brain and testicles) and it is not affected by bio distribution related factors. The regimen of TBI varies a significantly across institutions and the object of the ILROG guideline is to provide practice guidance for the current practice of TBI. This guideline provides information not only for dose, fractionation, number of daily fractions and planning specifications, but also the recommendations for patients' evaluation before TBI.

LUNG

ASTRO Guideline for palliative treatment of localized disease – use of chemoradiation for selected population

The American Society of Therapeutic Radiation Oncology (ASTRO) guideline update recommends the indications for palliative hypofractionated RT with concurrent chemotherapy. According to the 2018 guideline patients should be fit for chemotherapy, have an ECOG performance status of 0 to 2 and a life expectancy of at least 3 months. In this subset of patients, if radical curative treatment is unsuitable, moderate hypofractionated radiation should be offered with a concurrent platinum-containing chemotherapy. This approach is recommended by this guideline over treatment with either single modality alone⁽⁹⁾.

PALLIATIVE

Normgrams, treatment combination and ablative treatment on the oligometastatic setting – importance of patient selection.

Palliative care is an essential part of radiation therapy application. In the last decade, oncology practice has been evolving and it is now more challenging to define which patients will have prolonged survival to experience the benefits of more radical treatments. In addition, there is a clinical conundrum on which are the better schedules and technologies in a cost effective scenario. In this scenario, an accurate assessment of survival in the stage IV disease is particularly important thus prognostic tools are, though, useful for critical decisions in daily clinical practice.

An interesting study from Taiwan developed and validated a nomogram for assessing survival in patients with metastatic lung cancer referred to RT for bone metastases. The study endpoints were death within 3, 6 and 12 months. The tool provided clinical relevant grouping information that can assist radiation oncologists in tailoring treatment approaches to the patients' life expectancies, including initiating end of life discussions and/or hospice referrals at appropriate time⁽¹⁰⁾.

A systematic review from Netherlands was designed to identify prognostic factors that are associated with survival in patients with spinal bone metastases. Strong evidence for a positive association with survival was found for the primary tumor histology, performance status and American Society of Anesthesiologists (ASA) classification⁽¹¹⁾.

The association between RT and immunotherapy has been object of interesting insights also. An analysis of American National Cancer Database explored the clinical effect of this combination in patients with melanoma brain metastases. Although there is potential bias to the retrospective design, the median overall survival for patients treated with radiotherapy and immunotherapy was 11.1 months and 6.2 months for radiotherapy alone ($p < 0.05$)⁽¹²⁾.

The paradigm COMET-Trial, presented at 2018- ASTRO annual meeting, assessed the impact of delivering stereotactic ablative RT (SABR) compared to SOC on survival, oncologic outcomes, toxicity, and quality of life (QOL) in patients with a controlled primary tumor and up to five oligometastatic lesions. SABR was associated with an improvement in overall survival and progression free survival was doubled. Grade 2 toxicities were more common with SABR, but no differences were seen in QOL⁽¹⁾.

CONCLUSIONS

The year of 2018 was an active and important year for oncology and radiation oncology. The academic community combined efforts succeed to provide better evidence and application of RT in several tumor sites and also in the metastatic setting. It was shown that radiation oncology is in a unique interphase for oncology, surgery and others specialities. Finally, it has been shown that advances in technology are improving applications and quality of radiotherapy.

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