



## Defining the role of curative local therapy in oligometastatic cancer: a new era

Oligometastatic cancer is defined as a clinical state of metastatic disease that is limited to “oligo” or few metastatic lesions as identified by imaging. Conceptualized in the 1990s by Drs. Hellman and Weichselbaum, it has now become an accepted condition in the natural history of most solid malignancies. Historically, the primary approach of metastatic cancer treatment has been prolonging disease control with systemic therapy and palliating symptoms with medical management and radiotherapy. As the oligometastatic state moves beyond a hypothesis, questions on the optimal treatment and ultimate goals of care (including potential for cure) for these patients will arise. Unlike in widespread metastatic disease, where systemic therapy plays a pivotal role in controlling the systemic disease burden, for oligometastatic disease, the role of metastasis-directed local therapy with radiation therapy or surgery, in conjunction with systemic therapy, is crucial. Treatment in this situation has the potential to improve provide durable local control, delay the time to next-line systemic therapy, and even prolong survival, possibly with cure, by eradicating visible disease burden. This focused series, with ten timely and impactful articles, addresses the concept of oligometastases, the current status of published literature on the treatment of oligometastases, and the role of ablative radiation therapy for oligometastatic disease for various cancers.

The first article discusses the concept of oligometastases, and the history from which the hypothesis of the oligometastatic disease arose (1). A detailed discussion on the technical aspect of delivering such an ablative dose of radiotherapy for oligometastatic disease (2) sets the stage for the subsequent articles that delve into the treatment of oligometastases from specific cancer types or sites. The article by Mihai *et al.* provides a detailed description of the technology using linear accelerator (LINAC)-based stereotactic body radiation therapy (SBRT) [or stereotactic ablative radiotherapy (SABR)], and the necessary steps to develop a program where such service can be provided.

Lung cancer is the leading cause of cancer related mortality globally. While immunotherapy (IO) has made significant improvements in the outcomes of advanced non-small cell lung cancer (NSCLC), response rates to IO remain only modest, and the large majority of patients with advanced NSCLC die from their disease. Dohopolski *et al.* (3) review the treatment of oligometastases from NSCLC and how recent evidence from prospective studies have shown a survival benefit from using SBRT in this setting. With significant advancements in systemic therapy for breast cancer, a rationale combination of systemic therapy with locally ablative therapy for oligometastases carries more importance. Kent *et al.* (4) provide a detailed review of the role of SBRT in oligometastatic breast cancer. While there has been significant advancement made in curing localized prostate cancer using surgery and radiation therapy, many patients develop metastatic disease. Androgen deprivation remains the mainstay of initial therapy for metastatic prostate cancer, but eventually the disease becomes hormone refractory. The article by Sritharan *et al.* (5) reviews the current evidence not only for SBRT in oligometastatic prostate cancer but also usefulness of prostate-directed therapy in the presence of untreated prostate cancer with synchronous oligometastatic disease.

One of the early success stories of treating oligometastatic cancer combining both effective systemic therapy and local treatment was in colorectal cancers with liver metastasis found synchronously at the time of initial diagnosis. Chandy *et al.* (6) provide a historical overview of hepatic resection in the setting of *de novo* oligometastatic colorectal cancer. In addition, they provide a detailed description of management of these complex scenarios in the multidisciplinary setting, which is a key to the success of such an approach.

While in adults the treatment of oligometastatic cancer has gained a momentum, the concept and management of pediatric patients with oligometastatic disease are evolving. The next article by Smile *et al.* (7) provides an overview of current and future research in pediatric cancers with oligometastatic disease. Given that the pediatric population is particularly vulnerable to long-term radiation-induced toxicities, this article provides information on available evidence of such toxicities when an aggressive ablative radiation treatment approach is utilized.

The brain is one of the most common sites of cancer spread. Mounting data over the past two decades have shown that single-fraction stereotactic radiotherapy (SRS) can successfully control limited brain metastasis. The omission of whole brain radiation therapy does not impact survival and results in improved neuro-cognitive outcomes. The article by Chaung *et al.* (8) reviews the management of limited brain metastasis utilizing a stereotactic approach. The article also describes future

directions in studying SRS for patients with >10 brain metastasis as well as the potential effects of newer systemic therapy strategies in combination with SRS.

Looking to the future of oligometastatic disease management, the article by Turchan *et al.* (9) explores the role of IO in combination with SBRT. As clinical trials demonstrate benefits of IO for specific cancers, it will become important to explore and understand the role of radiation in combination with IO. Despite the successes of IO, the response rate is limited and many patients with initial response eventually progress. With ablative radiotherapy, there is a potential to augment the effect of IO, including with the potential for an abscopal effect (i.e., unanticipated response in lesions not targeted with radiation).

Finally, the article by Li *et al.* (10) summarizes ongoing clinical trials using SBRT in the oligometastatic setting.

In summary, stereotactic radiotherapy is an established technique of delivering ablative doses effectively and safely. Combining such ablative radiation with conventional systemic drugs and newer agents like IO is an active area of research for multiple cancers. The articles in this focused series provide the current evidence on the concept of oligometastatic disease and the use of SBRT for oligometastases. Additionally, future directions, including ongoing clinical trials, are highlighted throughout this special series. To better understand the oligometastatic state and the treatments that can optimally manage patients with oligometastases, further research is needed, with a focus on identifying those factors that best predict response to treatment and determining the optimal candidates for metastasis-directed local therapy.

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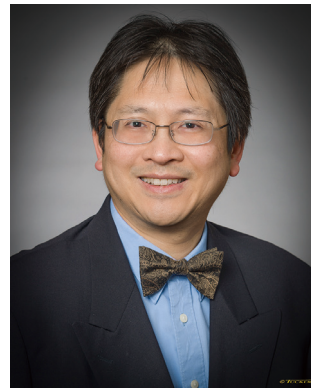
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