Charting new courses in palliative radiation therapy: Technology's role

Mary Beth Massat

Although advanced cancer, such as metastatic disease, cannot often be cured, it can be treated with palliative care. Designed to resolve symptoms and make patients as comfortable and pain-free as possible, palliative treatments include surgery, chemotherapy and radiation therapy.

The American Society of Clinical Oncology (ASCO) recommends that palliative care be offered to patients within 8 weeks of an advanced cancer diagnosis. A presentation at the 2015 annual meeting of the American Society for Radiation Therapy (ASTRO) reported that a collaborative, patient-reported outcomes-based approach by radiation oncologists and palliative care teams improved symptom management and lowered costs for late-stage cancer patients and end-of-life hospitalizations.[1]

In 2017, ASTRO updated its evidence-based guidelines for palliative radiation therapy (RT) of bone metastases. The updated guidelines address the 8 questions from the initial 2011 bone metastases guidelines based on new published clinical research and literature.

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According to Joshua Jones, MD, MA, assistant professor, Department of Radiation Oncology, Hospital of the University of Pennsylvania, and a co-author of the updated guidelines, one of the more common treatments is managing bone metastases.

"There is a range of what is appropriate, so we need the guidelines. But fundamentally, we need to … better understand how best to tailor radiotherapy to the individual patient: When is stereotactic radiotherapy and ablative radiotherapy most appropriate in the management of bone metastases, and when are simpler techniques with lower doses most appropriate?" he asks, noting that an influx of data is expected in the next two years from randomized studies. "The key questions are: Who will most benefit from palliative radiotherapy? What dose/fractionation and technique are most appropriate with de novo palliative radiation? What dose/fractionation and technique are most appropriate in the re-irradiation setting?"

The brain is another common site for metastatic cancer. ASTRO has published guidelines on whole-brain radiation therapy (WBRT) and stereotactic radiosurgery (SRS), as well as combining WBRT with radiosensitizers or chemotherapy. But even with these guidelines, ambiguity remains regarding the most optimal treatment, says Charles B. Simone, MD, associate professor at the University of Maryland School of Medicine, Baltimore, and medical director of the Maryland Proton Therapy Center. Dr. Simone believes it is possible to develop standard pathways for treatments based on factors such as number and/or volume of metastatic lesions.

However, other variables can determine the number of treatment approaches, such as patient performance status, extent of extracranial disease and overall tumor burden, neurological symptoms, and other concurrent treatments being used such as chemotherapy or immunotherapy, notes Dr. Simone. "It can also be something as simple as the distance from the patient's home to the treatment facility," he says.

Current Trends

Dr. Jones notes two interesting trends in treating bone metastases: the use of more hypofractionated treatments and the movement toward advanced techniques such as stereotactic body radiation therapy (SBRT).

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Charles B. Simone, MD
University of Maryland School of Medicine

he says, "where we are utilizing more complex techniques and also simpler, shorter treatments."

Fundamentally, the key question remains that of local control of the metastasis. Consider a patient with a painful rib metastasis and other metastatic disease that may benefit from additional systemic therapies. Given the equivalence in pain palliation with single- and multifraction RT, a simple treatment with 1 fraction could be the best course, says Dr. Jones. On the other end, a patient with a solitary metastasis in the spine that can worsen pain and potentially lead to spinal cord compression may be best served with an ablative technique, such as SBRT.

"We have to define upfront the goal of our therapy," he explains. "We traditionally thought of radiotherapy in two categories: curative or palliative therapy. Now we see that there is an intermediary goal: a patient with metastatic disease who we don't think we can cure but [for whom] there is a strong rationale for an aggressive approach to improve local control and decrease side effects."

In addition to increased use of more advanced treatment modalities such as intensity-modulated RT (IMRT), volumetric-modulated arc therapy (VMAT), SBRT and, in some cases, proton therapy, Dr. Simone sees two other trends in palliative RT: shorter treatment courses and high variations in outcomes.

"There is a recognition that a shorter course of therapy is equally effective, more cost effective and more convenient for patients," Dr. Simone says. "Also, there is great hetereogeneity among patients with metastatic cancer [and] considerable variability in outcomes according to primary tumor site and location, and extent of metastases.

For example, widely metastatic disease differs from a single oligometastatic disease for palliation. "We need to consider not only improving the quality of life but also … progression-free survival and potentially even overall survival," he says.

Metastatic location is crucial in determining type of treatment. With rib, pelvic or extremity metastatic disease, traditional 2- or 3-dimensional RT is generally simple and effective. In the brain, SRS is often utilized. In more critical areas, and particularly for patients with oligometastatic or oligoprogressive disease, advanced modalities such as IMRT and SBRT can be considered.

While proton therapy is not broadly used, it also can be an option. A key consideration is re-irradiation of a site in cases where the clinician cannot deliver radiation again due to maximum tissue constraints of the organ or anatomic area. For instance, a patient with a large bulky thoracic recurrence that had previously been treated with definitive RT, and where retreatment with additional photon RT would be too toxic, could be a candidate for proton re-irradiation to prevent or treat cord compression, improve quality of life, or locally control disease and delay additional progression or further systemic therapy. He recalls a patient with otherwise stable disease and good performance status who had two prior courses of RT for spinal metastases. The patient was referred for a third course of treatment using proton therapy to alleviate painful compression in the spine and to prolong survival. With proton therapy, Dr. Simone stopped the dose before it reached the spinal cord, allowing for effective re-irradiation and palliation.

Adds Dr. Jones, "While location matters, part of the answer to the question is prognosis. If a patient has been through 12 courses of systemic therapy and the disease is widespread, then local control is less likely to matter, and less complex treatments are generally the right course."

In addition to local control and prognosis, the clinician must also consider the most appropriate treatment for the desired effect, such as alleviating pain, a neurologic deficit, bleeding, cough or an obstruction.

Also being explored is the role of histology in tailoring palliative radiation therapy. Dr. Jones explains that if the tumor histology is understood to be more radiosensitive or radio-resistant to RT, that can impact techniques and dose.

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Joshua Jones, MD, MA
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"A question I often ask is, What else is possible for that patient so we aren't just thinking about radiotherapy? If we have the option for an interventional-directed ablation, or a surgical technique or effective systemic therapy, how do we weigh those in conjunction with RT?" he poses. "While some of this was addressed in the updated ASTRO guidelines, it is an area that we are still exploring."

Benefit vs cost is a concern as well. Dr. Jones had a patient who, in her own words, had crushing medical debt and couldn't catch up. Her main concern as she approached end of life was the impact of the debt on her family.

Barriers

One barrier to providing effective palliative radiation therapy is patient pain. In Dr. Jones' practice, nearly one-third of his patients have difficulty lying flat on a treatment table due to painful spine, rib or bone metastases. To address this problem, continued development is needed for technologies that can rapidly scan and treat a patient. Dr. Jones would also like to see more innovation in treatment delivery, such a seated position for treatment.

"We have a tremendous opportunity to come up with alternative patient positioning as well as imaging modalities in palliative radiation," he stresses.

Unfortunately, the most common barrier to initiating hypofractionated RT or SBRT for palliative care is the clinician's comfort level. "They know the data and information published in the literature," says Dr. Jones, "but if they've never done it, they are hesitant."

A key predictor of using a shorter course of treatment is clinician training. While palliative RT has been used for decades, the field has evolved just as it has with curative RT. "As a society, we need to think about how we continue to make palliative care a part of our practice, including how our treatments impact our patients," he adds.

Similarly, Dr. Simone says continuing education is critical to increasing use of hypofractionated and single-fraction treatments, noting that the updated ASTRO guidelines for bone metastases cite pain relief equivalency between single and multiple fraction regimens.

"Another barrier is the misalignment between the goals of the patient and the physician," says Dr. Simone. In general, predicting overall survival remains a difficult process. Yet, while a patient may be terminally ill and desire quality of life, the clinician may hope that the course of treatment can impact survival.

"Examining quality of life should not just be the end result of symptoms but also impact how we deliver treatments," he adds. "I am definitely an advocate of a shorter course of treatment for palliation and, whenever possible, will prescribe a single or hypofraction RT treatment."

To address the need for training, Dr. Simone is hopeful that more residency programs will include dedicated curriculums for palliative care. Instituting a dedicated palliative radiation oncology service can also impact the use of single-fraction and hypofractionated radiation therapy for bone metastases, as was recently shown following initiation of the Supportive and Palliative Radiation Oncology service at the Dana-Farber/Brigham and Women's Cancer Center Department of Radiation Oncology.[2]

Fortunately, such programs have increased over the last 5 years, "While experience is still limited, the evidence shows that having a dedicated program increases referrals and the ability to study all these issues surrounding palliative care," says Dr. Jones. "I hope this trend continues, with a focus on both simple and complicated stereotactic techniques, so we can continue to explore what is best for these patients."

References

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