Stereotactic Radiotherapy: An Emerging Treatment for Spinal Metastases

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ABSTRACT: Aim: The purpose of this concise update is to describe the emerging treatment of stereotactic body radiotherapy (SBRT) for spinal metastases. Rationale: Spinal metastases are common and can present complex clinical challenges that conventional treatment cannot always meet satisfactorily. Examples include a history of prior irradiation at the same site or radio-resistant tumor histology. Stereotactic body radiotherapy makes it possible to deliver high doses of radiation with the aim of improving tumor control and palliation. It is increasingly being offered to selected patients including those requiring re-irradiation and post-operative treatment. Conclusion: It is important that specialists managing patients with spinal metastases are aware of the potential advantages of SBRT and how this can complement and extend existing treatment approaches, including spinal decompression and stabilization.

Spinal metastases occur in up to 40% of cancer patients, often cause back pain, and if untreated can result in the medical emergency of malignant epidural spinal cord compression. Conventional external beam radiotherapy (RT) treatments using short-course low-dose radiation, such as 8 Gray (Gy) in a single fraction or 20 Gy in five daily fractions, are aimed primarily at pain control. Radiotherapy is the most common treatment for spine metastases. However, selected patients with oncological spinal instability or neural compression should be considered for spinal surgery which is optimally combined with post-operative RT1,2.

Stereotactic body radiotherapy (SBRT) has recently emerged as an alternative, more aggressive, treatment option to conventional RT for selected patients with spinal metastases. Stereotactic body radiotherapy has resulted from rapid technologic advances in radiation oncology, in particular intensity modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT). The former makes it possible to shape radiation dose around a small target while sparing adjacent critical structures, including central structures within the target perimeter, such as the spinal cord (Figure 1). The latter allows the radiation to be delivered with millimetre precision3. This means that the dose to the vertebral tumor can now be escalated whilst maintaining a safe dose-limit to the spinal cord4. The objective of radiation therapy, therefore, has shifted from one primarily aimed at pain relief to long-term local tumor control5.

What is stereotactic spine radiotherapy?

Spine SBRT typically refers to the precise delivery of one to five fractions of high dose radiation to the tumor while sparing the surrounding normal tissues, and doses have ranged from 16-24 Gy in a single fraction to 20–40 Gy in two to five fractions5. Figure 1 illustrates the fundamental difference between conventional RT and intensity modulated SBRT treatment plans. The highly shaped dose distribution generated by intensity...
modulated radiation permits dose escalation within the target and a rapid dose fall-off beyond the target edges, enabling sparing of the surrounding normal tissues. Treatment volumes are typically limited to the gross tumor volume with or without part, or all, of the remaining vertebral segment. This is unlike conventional RT in which one or two simple RT fields are used to treat at least one healthy vertebral body above and below the disease, in order to ensure sufficient dose is delivered to the tumor. To meet the increased demands of accurate tumor delineation and identification of the organs-at-risk (e.g. the spinal cord, esophagus, lungs, kidneys), spine SBRT treatment planning places greater emphasis on imaging than conventional RT. Spine SBRT routinely requires both thin slice computed tomogram (CT) and magnetic resonance imaging (MRI) for treatment planning (Figure 2), and PET-CT and CT-myelography may also be helpful.

**How is stereotactic spine radiotherapy delivered?**

Computerized planning systems design and calculate the RT dose distribution using, for example, fixed-multiple field IMRT...
or rotational IMRT (volumetric modulated arc therapy). To make it possible to deliver treatment with an overall accuracy of 1-2 mm, IGRT is used to verify the position of the target and critical structures just prior to and during radiation delivery. One commonly used IGRT modality is cone-beam CT (CBCT). This consists of an isocentric fluoroscopic CT unit mounted on the linear accelerator (radiation delivery unit). An example of the IGRT process using CBCT is shown in Figure 3. Unlike x-rays, which image bony anatomy in two dimensions, CBCT provides three dimensional volumetric images of both bone and to some extent soft-tissues, thus aiding target and organ-at-risk localization for precise delivery.

Patient selection for stereotactic spine radiotherapy and potential toxicities

Spine SBRT is more complex and resource intensive than conventional RT with stringent requirements for treatment planning and delivery. Patient selection and multidisciplinary evaluation are important. Consultation with spine surgeons is often necessary to consider surgical options to correct critical neural compression or spinal instability before SBRT. Stereotactic body radiotherapy has most often been used for metastases less than three adjacent vertebral bodies in length, and when tumor is at least 1-2 mm away from the spinal cord in order to avoid under-dosing or missing epidural disease.

Although spine SBRT is usually well tolerated possible side effects include short-term fatigue, pain flare (a transient increase in pain shortly after radiotherapy), skin reactions and nausea. Important long-term consequences have been described following spine SBRT including vertebral compression fractures that may be associated with pain and, rarely, radiation myelopathy which at its worst can lead to irreversible paralysis.

Current indications and evidence in support of spine SBRT

Presently, spine SBRT is most often used in the treatment of patients with a good performance status/Karnofsky score, a limited extent of metastatic disease, and ‘radio-resistant’ tumor histology (e.g. renal cancer). This technique is also particularly useful in patients requiring re-irradiation, as there may be limited or no further options using conventional RT. The current evidence is limited to a growing body of retrospective single institution series and a few non-randomized prospective studies. Initial rates of pain response and imaging-based local control are encouraging, and range anywhere from 80-95% in the primary, re-irradiation and post-operative scenarios. This compares with overall rates of pain response in bony metastases (not just spine) of approximately 60% for both single and multi-fraction conventional RT schedules. Metastases with a defined paraspinal component (disease that has extended beyond the vertebrae) may stand to gain most from SBRT, as local control rates of only 46% at one-year and 39% at two-years have recently been reported with conventional RT alone.

Before making firmer conclusions we await with interest the outcome of the recently initiated randomized controlled study (RTOG 0631) comparing spine SBRT to conventional RT in patients with no prior radiation and symptomatic localized spinal metastases.

Future developments

Traditional surgery consists of an open invasive approach which is associated with significant post-operative morbidity. However, there have been recent developments in image-guided and minimally invasive spine surgery for metastases which include, for example, minimal access spine surgery using microsurgical techniques and percutaneous pedicle screw fixation or vertebral augmentation techniques such as vertebroplasty/kyphoplasty, that are aimed at reducing morbidity. Combining post-operative SBRT with new surgical approaches to achieve spinal cord decompression and mechanical stabilization not only allows for the goals of surgery to be met, but may also result in durable long-term tumor control.

Spine SBRT may also play an important role in patients with oligometastatic disease (e.g. five or fewer sites of metastasis throughout the body). It is thought that aggressive management
of metastatic disease in these patients with ablative local therapies may result in long-term survival for selected patients. This is now an active area of investigation in cancer management.

**Key points**

(1) There are limitations to using conventional RT for spinal metastases, in particular, for patients who require re-irradiation.

(2) Spine SBRT is an advanced treatment technique that allows spinal metastases to be treated to a higher dose than would otherwise be possible whilst respecting the tolerance of the surrounding critical normal tissues.

(3) The body of evidence supporting spine SBRT consists predominantly of heterogeneous patient populations and retrospective single institution series, however, overall spine SBRT has demonstrated promising efficacy and safety.

(4) Patients with neural structure compression or spinal instability should have a surgical opinion prior to deciding upon SBRT.

(5) There is increasing interest in combining novel less invasive surgical approaches with spine SBRT.

**DISCLOSURES**

Max Dahele: VU University Medical Centre has research collaborations with Varian Medical Systems, USA; BrainLAB AG, Germany and Velocity Medical Solutions, USA. Travel support from BrainLAB.

**REFERENCES**