Critical Reviews in Oncology/Hematology 98 (2016) 147–158

Contents lists available at ScienceDirect

Critical Reviews in Oncology/Hematology

journal homepage: www.elsevier.com/locate/critrevonc

Review

Spinal metastases: Is stereotactic body radiation therapy supported by evidences?

Berardino De Bari[a,*], Filippo Alongi[b], Gianluca Mortellaro[c], Rosario Mazzola[b,c], Schiappacasse Luis[a], Guckenberger Matthias[d]

[a] Radiation Oncology Department, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland
[b] Radiation Oncology Department, Sacro Cuore-Don Calabria Hospital, Negrar-Verona, Italy
[c] Radiation Oncology Department, University of Palermo, Palermo,Italy
[d] Department for Radiation Oncology, University Hospital Zurich, University of Zurich, Zurich, Switzerland

Contents

ARTICLE INFO

Article history:
Received 24 September 2015
Received in revised form 1 November 2015
Accepted 4 November 2015

Keywords:
Spine metastases
SBRT
Dosimetry
Palliative radiotherapy
Local control
Toxicity

ABSTRACT

Stereotactic body radiotherapy (SBRT) is becoming widely adopted in the treatment of primary and secondary tumors. Spinal bone metastases are frequently discovered in cancer patients, and in the past have been usually treated with a palliative goal. Nevertheless, in some particular clinical settings, such as oligometastatic patients and/or those with a long life expectancy, spinal SBRT could be considered a valid therapeutic option to obtain long-lasting palliation and, when possible, with a curative goal.

This review aims to summarize available clinical and dosimetric data of published studies about spinal SBRT.

1. Introduction

Approximately one third of all cancer patients will develop bone metastases and approximately 70% will present metastases involving the vertebral column, most commonly at the thoracic and the

* Corresponding author at: Radiation Oncologist, fESTRO, Centre hospitalier universitaire vaudois (CHUV), Service de radio-oncologie, Bâtiment hospitalier, Rue du Bugnon 46, CH-1011 Lausanne, Switzerland. Fax: +41 21 314 46 01.
E-mail address: berardino.de-bari@chuv.ch (B. De Bari).

http://dx.doi.org/10.1016/j.critrevonc.2015.11.002
1040-8428/

lumbar level (Van Oorschot et al., 2011). Back pain is the most common initial presenting symptom, often with associated neurological problems. Conventional fractionated radiotherapy (RT) has an historical role in the management of spine metastases and the most commonly used regimen of RT is 30 Gy in 10 fractions (De Bari et al., 2011). Nevertheless, a RTOG study evaluating different dose fractionation schedules in terms of frequency, promptness and duration of pain relief showed that more hypofractionated schedules were as effective as high dose protracted regimens (Tong et al., 1982). These data have been confirmed in several randomized controlled trials and subsequent meta-analyses conducted by Wu et al. and by Chow et al., both showing no significant differences in complete and overall pain relief between single and multi-fractions palliative RT for bone metastases, but also significantly higher re-treatment rates occurring in patients receiving single fraction regimens (Wu et al., 2003; Chow et al., 2012). The choice between the different schedules depends on several factors, including the clinical conditions of the patient and/or the local anatomy and/or some local organizational constraints (Koswig and Budach, 1999). However, single-dose treatments are usually preferred in patients with a limited lifespan and/or poor performance status or in case of long waiting lists of the treating centers (Lutz et al., 2007).

Recent advances in RT treatment planning and dose delivery allow radiation oncologists to deliver treatments with a long-lasting palliation potential (and sometimes also potentially curative) also to patients that would be traditionally candidates only to palliative systemic therapies, possibly at a reasonable price in terms of toxicity. Ideal candidates for these treatments are *oligometastatic* (i.e. those presenting 1–5 metastatic sites and also an active primary lesion) or, much better, *oligo*-recurrent patients (i.e. patients affected by 1–5 metastatic sites with a cured primary tumor) (Niibe and Chang, 2012).

A study by Jacobson et al. (2001) already showed that patients with bony oligometastases may have a prolonged survival time, passing from a median survival of 55 months for patients with 1 bone metastatic site to 22 months for those presenting $\geq$3 metastatic sites. Moreover, a curative approach to metastatic disease could potentially allow a durable tumor control, following the "seed and soil" and the "multiple steps cancer progression" theories (Chambers et al., 2002; Fidler, 2003).

Recently, stereotactic body radiation therapy (SBRT) has been introduced in the daily clinical practice in several RT centers, both in the treatment of small primary and secondary tumors and represent a local, non-invasive approach compared to surgery or other minimal-invasive options because of a lower rate of morbidity, lower costs, and the potential for delivering ablative treatments on an outpatient basis (De Bari et al., 2014a; Alongi et al., 2013, 2012; Ricardi et al., 2013). SBRT was introduced in the 1990s, as an extracranial application of the well-known radiosurgery approach using spatial coordinates to define the position to irradiate target with highly escalated radiation doses. Today, the concept is rapidly changing, and SBRT identifies a "philosophy" for treating cancer in the body not necessarily with spatial coordinates, but essentially prescribing high focused high total doses delivered in one or few sessions (Ricardi et al., 2013; Alongi et al., 2014). Moreover, the introduction over the last few decades, of intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT) techniques allowed clinicians to prescribe safely higher doses/fraction in few fractions. Several studies showed a reduction of toxicity rates in patients treated with IMRT compared to those treated with 3D-EBRT (Gomez-Millan et al., 2013; Bauman et al., 2012). Recently, more evolved forms of IMRT, such as volumetric modulated arc radiotherapy (VMAT) or helicoidal tomotherapy (HT), and robotic accelerators specifically designed for SBRT have been introduced in the clinical practice, showing initial promising dosimetric improvements compared to IMRT (Mellon et al., 2015; Dai et al., 2014; Peters et al., 2014; Atalar et al., 2012; Cendales et al., 2014) combined with substantially reduced treatment delivery times. Image guided radiotherapy (IGRT) allowed daily online and offline verification of the setup of the patients. Using IGRT, the treatment volume can be reduced by minimizing the size of the necessary margins to count for inaccuracies in target position and patient setup, with a consequent reduction of toxicity rates (Alongi and Di Muzio, 2009; De Bari et al., 2014b; Maund et al., 2014; Chen et al., 2014; Udrescu et al., 2012). Spine SBRT has been quickly adopted in the RT community (Pan et al., 2011), and available retrospective and prospective evidences are growing, both in terms of number of involved patients and in the quality of the studies (Wang et al., 2012; Ryu et al., 2003; Guckenberger et al., 2014).

This review aims to perform a descriptive summary of the available clinical data and dosimetric aspects of SBRT for spinal metastases.

2. Studies selection

Articles dealing with SBRT in the treatment of spinal metastases have been searched. The word "SBRT" or "stereotactic body radiotherapy" or "stereotactic body radiation therapy" AND "spinal metastases" or "metastases" were used to search articles in the PubMed database. Then, articles reporting data concerning issues other than the role of SBRT in the treatment of spinal metastases were excluded. Articles written in languages other than English and those presented only as abstracts at conferences proceedings were also excluded. Finally, 24 articles were selected (for a total of 2792 patients and 3454 metastatic lesions, see Table 1).

3. Clinical experiences: clinical outcomes and safety

3.1. Efficacy

The first report about SBRT for spinal metastases was published in 1995 by Hamilton et al. (1995). Authors used a prototypic device called extracranial stereotactic radiosurgery frame to deliver SBRT to treat 5 patients with metastatic spine neoplasms using a modified linear accelerator. This system had been presented by the same authors in a previous report (Hamilton and Lulu, 1995) and it was used both for immobilization of the patients, and for tumor localization and treatment. A median single fraction dose of 10 Gy (range: 8–10 Gy) was delivered, with a median normalization to 80% isodose contour (range: 80–160%). These five patients represent the first clinical application of SBRT for spinal targets. After a median follow-up of 6 months (range: 1–12), authors reported a single complication of esophagitis resolved with medical therapy in a patient treated for a tumour involving the C6-T1 segments. No radiographic or clinical signs of in-field progression were reported, but 2 patients died from systemic metastatic disease. The authors concluded that extracranial SBRT could be considered a therapeutic option, even in case of spinal cord compression. Since then, several articles have been published.

3.2. Clinical outcomes

Tables 1 and 2 summarize available data (Wang et al., 2012; Guckenberger et al., 2014; Gerszten et al., 2007; Sellin et al., 2015; Folkert et al., 2014; Mantel et al., 2014; Benzil et al., 2004; Chang et al., 2007, 2009, 2012; Choi et al., 2010; Gagnon et al., 2009; Sheehan et al., 2009; Zelefsky et al., 2012; Greco et al., 2011; Garg et al., 2012; Nguyen et al., 2010; Sahgal et al., 2009; Yamada et al., 2008; Klish et al., 2011a; Balagamwala et al., 2012; Schipani et al., 2012 ; Laufer et al., 2013a; Heron et al., 2012). In Table 1, the number