

## Clinical Study

# Spinal instability as defined by the spinal instability neoplastic score is associated with radiotherapy failure in metastatic spinal disease

Merel Huisman, MD<sup>a,\*</sup>, Joanne M. van der Velden, MD<sup>a</sup>, Marco van Vulpen, MD, PhD<sup>b</sup>, Maurice A.A.J. van den Bosch, MD, PhD<sup>a</sup>, Edward Chow, MBBS<sup>c</sup>, F. Cumhur Öner, MD, PhD<sup>d</sup>, Albert Yee, MD<sup>e</sup>, Helena M. Verkooijen, MD, PhD<sup>a</sup>, Jorrit-Jan Verlaan, MD, PhD<sup>d</sup>

<sup>a</sup>Department of Radiology, University Medical Center Utrecht, Heidelberglaan 100, 3508 GA Utrecht, The Netherlands

<sup>b</sup>Department of Radiation Oncology, University Medical Center Utrecht, Heidelberglaan 100, 3508 GA Utrecht, The Netherlands

<sup>c</sup>Department of Radiation Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, 2075 Bayview Avenue, Toronto, Ontario M4N 3M5, Canada

<sup>d</sup>Department of Orthopedic Surgery, University Medical Center Utrecht, Heidelberglaan 100, 3508 GA Utrecht, The Netherlands

<sup>e</sup>Department of Orthopedic Surgery, Sunnybrook Health Sciences Centre, University of Toronto, 2075 Bayview Avenue, Toronto, Ontario M4N 3M5, Canada

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**Abstract**

**BACKGROUND CONTEXT:** Although radiotherapy is effective in achieving pain relief in most patients, it is not completely understood why some patients respond well to radiotherapy and others do not. Our hypothesis was that metastatic bone pain, if predominantly caused by mechanical instability of the spine, responds less well to radiotherapy than metastatic bone pain caused by local tumor activity. Recently, the spinal instability neoplastic score (SINS) was proposed as a standardized referral tool for nonspine specialists to facilitate early diagnosis of spinal instability.

**PURPOSE:** To investigate the association between spinal instability as defined by the SINS and response to radiotherapy in patients with spinal metastases.

**STUDY DESIGN:** A retrospectively matched case-control study in an academic tertiary referral center, conducted according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

**PATIENT SAMPLE:** Thirty-eight patients with spinal metastases who were retreated after initial palliative radiotherapy from January 2009 to December 2010 were matched to 76 control patients who were not retreated.

**OUTCOME MEASURES:** Radiotherapy failure as defined by retreatment (radiotherapy, surgery, and conservative) after palliative radiotherapy for spinal metastases.

**METHODS:** Radiotherapy planning computed tomography scans were scored by a blinded spine surgeon according to the SINS criteria. The association between SINS and radiotherapy failure was estimated by univariate and multivariate conditional logistic regression analysis.

**RESULTS:** Median SINS was 10 (range 4–16) for cases and 7 (range 1–16) for controls. The SINS was significantly and independently associated with radiotherapy failure (adjusted odds ratio, 1.3; 95% confidence interval, 1.1–1.5;  $p=.01$ ).

**CONCLUSIONS:** This study shows that a higher spinal instability score increases the risk of radiotherapy failure in patients with spinal metastases, independent of performance status, primary tumor, and symptoms. These results may support the hypothesis that metastatic spinal bone pain, predominantly caused by mechanical instability, responds less well to radiotherapy than pain mainly resulting from local tumor activity. © 2014 Elsevier Inc. All rights reserved.

**Keywords:**

Spinal metastases; Spinal instability neoplastic score; Radiotherapy; Retreatment; Pain; Palliative care

FDA device/drug status: Not applicable.

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\* Corresponding author. Department of Radiology, University Medical Center Utrecht, Heidelberglaan 100, 3508 GA Utrecht, The Netherlands. Tel.: (31) 88-7556689; fax: (31) 30-2581098.

E-mail address: [m.huisman-7@umcutrecht.nl](mailto:m.huisman-7@umcutrecht.nl) (M. Huisman)

## EVIDENCE & METHODS

### Context

The authors postulate that metastatic bone pain, caused by instability, responds less well to radiotherapy than that resulting from local tumor activity. To test this hypothesis, a retrospective case-control study was conducted using the Spinal Instability Neoplastic Score (SINS).

### Contribution

Among a total of 114 patients (38 cases and 76 controls) the authors found that SINS grading was statistically associated with the necessity for further treatment following radiotherapy.

### Implications

This effort is a retrospective study and, importantly, the SINS grading was also conducted as part of the post-hoc analysis. As a result, the authors' contention is more correctly presented as patients necessitating further treatment following initial radiotherapy were found to have a statistically higher SINS grade. This type of study cannot show causation and the authors seem to present the SINS grade as a prognostic tool. Such utilization cannot be supported by this work. A more judicious approach would be to assign the SINS grade prospectively and then evaluate outcomes following the course of care.

—The Editors

## Introduction

In patients with metastatic bone disease, the spine is the most commonly affected site [1,2]. Signs and symptoms frequently associated with spinal metastases are pain, deformity, and neurologic deficits. To reduce pain and restore or maintain ambulation, radiotherapy is administered, sometimes in combination with surgery. Currently, the choice of therapy is not standardized and depends on several factors, including neurologic and functional status, spinal stability, life expectancy, and primary tumor site [3,4]. In general, surgical stabilization is indicated in case of gross spinal instability, neurologic deterioration during or after radiotherapy, and in selected cases of spinal cord compression [5,6]. In most institutions, spine surgeons evaluate the degree of spinal instability based on patient history, physical and radiologic examinations, and clinical experience [3,7]. As biomechanical stability of the spinal column can be difficult to assess, especially for nonspine surgeons, potentially unstable lesions may not always be recognized [3,8]. To create a simple standardized referral tool for nonspine specialists, the Spine Oncology Study Group developed the spinal instability neoplastic score

(SINS) [3]. The SINS is a scoring system based on clinical and radiologic findings and ranges from 0 to 18 points; higher total scores indicate more severe instability. Patients with a SINS of 7 or higher are presumed to have (potentially) unstable lesions and should be referred to a spine surgeon [3,7]. In its categorized form, SINS divides patients into three categories: stable (0–6 points), potentially unstable (7–12 points), and unstable (13–18 points) [3,7]. Spinal instability is associated with development of neurologic deficits, mechanical pain, and progressive deformity [7,9]. Early recognition of impending instability may, therefore, prevent painful collapse and loss of function by timely referral and treatment [3]. Presently, it is unclear whether spinal instability impairs outcome after radiotherapy [6]. We hypothesize that metastatic spinal bone pain predominantly caused by mechanical instability responds less well to radiotherapy than pain resulting from local tumor activity. The purpose of this matched case-control study was to investigate the association between spinal instability as defined by the SINS and response to radiotherapy in patients with spinal metastases.

## Methods and materials

### Patient selection

Between January, 2009 and December, 2010, a total of 712 patients underwent external beam radiotherapy for spinal metastases at the department of Radiation Oncology of the University Medical Center Utrecht, Utrecht, The Netherlands (an academic tertiary referral center). Patients were excluded if they had received previous surgery or radiotherapy to the same anatomic site or if they had already been referred to a spinal surgeon for the index lesion. We also excluded patients with nonstandard radiotherapy regimens (standard fractionations are 1×8 Gy or 5×4 Gy in our institution), patients with sacral or intramedullary index lesions, and patients with multiple spinal radiation fields. In patients with multiple index lesions, it was assumed that assessment of symptoms would be ambiguous. Of the remaining 373 patients, medical records were reviewed and radiotherapy failure occurred in 38 patients. Radiotherapy failure was defined as retreatment for clinical symptoms originating from the index lesion based on patient history, clinical examination, and imaging. Patients with radiotherapy failure will further be referred to as *cases*. All patients were seen by a radiation oncologist before treatment and for treatment follow-up. At the time of the study period, patients were not routinely evaluated for spinal instability by the radiation oncologist. Consultation of a spine surgeon was done at the discretion of the radiation oncologist. Retreatment consisted of reirradiation in 79% of cases (n=30), surgery in 10.5% of cases (n=4), and conservative management (implantation of intrathecal pump or immobilization with plaster jacket) in 10.5% of cases (n=4). In all surgically or

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