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# Staging of osteonecrosis of the jaw requires computed tomography for accurate definition of the extent of bony disease

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#### Abstract

Management of osteonecrosis of the jaw associated with antiresorptive agents is challenging, and outcomes are unpredictable. The severity of disease is the main guide to management, and can help to predict prognosis. Most available staging systems for osteonecrosis, including the widely-used American Association of Oral and Maxillofacial Surgeons (AAOMS) system, classify severity on the basis of clinical and radiographic findings. However, clinical inspection and radiography are limited in their ability to identify the extent of necrotic bone disease compared with computed tomography (CT). We have organised a large multicentre retrospective study (known as MISSION) to investigate the agreement between the AAOMS staging system and the extent of osteonecrosis of the jaw (focal compared with diffuse involvement of bone) as detected on CT. We studied 799 patients with detailed clinical phenotyping who had CT images taken. Features of diffuse bone disease were identified on CT within all AAOMS stages (20%, 8%, 48%, and 24% of patients in stages 0, 1, 2, and 3, respectively). Of the patients classified as stage 0, 110/192 (57%) had diffuse disease on CT, and about 1 in 3 with CT evidence of diffuse bone disease was misclassified by the AAOMS system as having stages 0 and 1 osteonecrosis. In addition, more than a third of patients with AAOMS stage 2 (142/405, 35%) had focal bone disease on CT. We conclude that the AAOMS staging system does not correctly identify the extent of bony disease in patients with osteonecrosis of the jaw.

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#### Introduction

Osteonecrosis of the jaw is a potentially severe side effect of antiresorptive agents including aminobisphosphonates and denosumab, the incidence of which is reported to vary from 0 to 27.5% in patients treated with bisphosphonates intravenously, with a mean incidence of 7%. It typically presents with areas of necrotic avascular jawbone exposed through the oral mucosa or facial skin.<sup>2</sup> Infection of necrotic bone is common and can lead to chronic pain, facial disfigurement, impaired function, and reduction of quality of life.<sup>3</sup> Management of osteonecrosis of the jaw is challenging and there is little evidence about the effectiveness of treatments. In most cases, the outcome is unpredictable. <sup>4</sup> Patients with mild to moderate disease are usually offered minimally invasive treatment such as control of infection and pain, and superficial debridement of bone, whereas it has been suggested that those with advanced and refractory disease may benefit from resection. <sup>2,5</sup> Accurate staging is therefore crucial to making therapeutic decisions and planning.

Staging of osteonecrosis of the jaw is currently based on the classification proposed by the American Association of Oral and Maxillofacial Surgery (AAOMS), which relies on clinical and radiographic examinations.<sup>2</sup> Other classifications are similarly based. <sup>6,7</sup> However, visual inspection is likely to identify only superficial signs, which may not necessarily reflect the true extent of bony disease. <sup>6,8,9</sup> For instance, the non-exposed variant, which often presents with minimal superficial clinical changes (such as a sinus tract), can be associated with widespread underlying necrosis of the iaw. 10,11 Signs such as exposed bone, infection with mucosal erythema, purulent discharge, and pain, however, may not be associated with widespread bony disease. 12 Studies have also shown that routine dental radiographs (such as panoramic radiography) is inferior to other imaging techniques in detecting the extent of bony disease in osteonecrosis. 13 A new

staging system has been proposed that integrates clinical manifestations and CT findings. <sup>14</sup> As the amount of research grows, an increasing number of authors now report the use of CT to study the extent of osteonecrosis in these patients. <sup>15-17</sup> There is, however, little evidence to suggest that the benefits of CT are enough to justify its routine use for staging of disease.

To test the hypothesis that the current staging system for osteonecrosis of the jaw may not correctly identify the extent of disease because of the lack of data from CT, we evaluated the agreement of AAOMS staging with CT imaging for assessment of the extent of bone disease (focal compared with diffuse).

#### Patients and methods

Design of the study

We performed a multicentre retrospective study known as MISSION ( $\underline{\mathbf{M}}$ ulticentre study on phenotype, def $\underline{\mathbf{I}}$ nition and cla $\underline{\mathbf{SS}}$ ification of oste $\mathbf{ON}$ ecros $\underline{\mathbf{I}}$ s of the jaws associated with bisphosph $\mathbf{ON}$ ates).

Setting

Research workers from the Universities of Verona, Palermo (Italy), and University College London (UK), designed the study and sent a collaboration proposal to a network of Italian centres of Oral Medicine and Oral and Maxillofacial Surgery with a special interest in the diagnosis and management of osteonecrosis of the jaw. The main requirements for participation were availability of a large group of patients with osteonecrosis, and routine use of CT in their investigations. Ten centres replied and agreed to collaborate, so a total of 13 centres contributed to the MISSION study. The ethics

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