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## Bisphosphonate-related osteonecrosis of the jaws of dental origin

To the Editor:

With reference to the Letter to the Editor regarding the article “Bisphosphonate-related osteonecrosis of the jaws: spontaneous or dental origin?”<sup>1</sup> we would like to thank the authors for their kind words, opinions, and suggestions. We agree with the authors on BRONJ being of dental origin, caused not only by dental procedures but also by dental pathology, as our article states.

We agree on their “outside-in” theory. There is no spontaneous origin; an infection causes the BRONJ from the oral cavity into the jaws. It can start with traumatized oral mucosa caused by ill-fitting dentures, knife-edge ridge mandibles, or a pronounced linea oblique externa, but it can also start with extractions, periodontal disease, or root canal problems, as mentioned in the article. That is also why in our opinion with early and thorough surgical treatment<sup>2-5</sup> it is possible to cure patients. Vice versa, this knowledge—BRONJ having a dental origin—also implies that having a good dental status or a well-fitting prosthesis may prevent luxation of BRONJ in patients using bisphosphonates (as described above).

The results of Landesberg et al.<sup>6,7</sup> may support our statement, but their research was based on very specific laboratory research on bone metastases, bone metabolism, and the migration of oral keratinocytes in vitro (with cells from mice and later on in primary human epithelial cells). These different studies show the same result: Bisphosphonates seem to be cytotoxic or tend to induce apoptosis in vitro, but the question remains how they establish that effect in vivo,<sup>6,7</sup> for the bisphosphonates are built-in in bone and not in mucosal cells. Although it has been suggested that gingival crevicular fluid should contain similar concentrations of

bisphosphonates as bone, there are still no data that can support that.<sup>8</sup> Therefore, further research is needed on this subject.

We disagree on the last suggestion, though. We stated that bisphosphonates stabilize the osteoporotic process and inhibit further tumor growth and metastasis in bone mainly by inhibiting bone resorption. That is how we meant the statement.

Bisphosphonate-related osteonecrosis of the jaws is a growing problem; after a difficult start, it has a better treatment and prevention outlook with the knowledge of the “outside-in” theory than it had with the former “spontaneous origin” theory.

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