Bone Scintigraphy and SPECT in the Evaluation of the Osseointegrative Response to Immediate Prosthetic Loading of Endosseous Implants: A Pilot Study

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Purpose: *Several recent medical reports have focused attention on the possible application of skeletal scintigraphy imaging in odontostomatology. The aim of the present report was to assess the influence of immediate prosthetic loading on peri-implant osteoblastic activity through bone scintigraphy.* ***Materials and Methods:*** *Implants were placed in 2 healthy women. A nuclear medicine investigation with single-photon emission-computed tomography (SPECT) was performed for both patients at 30 and 90 days after implant placement. The study was completed with acquisitions of planar images of the skull in an anterior view and the use of regions of interest (ROIs) of the same size in the area corresponding to immediate loading and in the opposite hemimandible (at the control sites). Count density ratios (counts/pixel) obtained from each ROI were used for a quantitative/relative assessment. Tomographic images were evaluated with a qualitative method. The spatial resolution of the reconstructed tomograms and of the planar images was approximately 7 mm.* ***Results:*** *Routine planar methodology provided a direct measure of cellular activity of the examined areas. The difference in count density ratio registered from the same ROI between the first and the second scintigraphy revealed the course of peri-implant osteoblastic activity, which was very high in the first month and then declined during subsequent months.* ***Discussion and Conclusion:*** *In spite of the small number of involved patients, the results obtained from this pilot study suggest that nuclear medicine may hold possible advantages in implant dentistry for those who seek to clarify the still unknown aspects of osteoblastic activity.* INT J ORAL MAXILLOFAC IMPLANTS 2004;19:80–86

Key words: *bone scintigraphy, dental implants, immediate loading, osseointegration, single-photon emission-computed tomography*

Several recent medical reports have focused attention on the possible application of osseous imaging in odontostomatology.[1–11] They assessed cellular activity of maxillary bone after the placement of dental implants or bone grafts with the aid of conventional-type nuclear medicine investigation and/or single-photon emission-computed tomography (SPECT) methods.

In 1997, Cervelli and coworkers suggested the use of SPECT methods for the long-term evaluation of the osseointegration process related to intraoral and extraoral implants and performed medical nuclear investigation with technetium-99m (99mTc) on 25 patients at 3 weeks and 3, 6, 12, and 24 months after implant placement.[2] This study showed the presence of peri-implant osteoblastic activity that peaked 3 weeks after surgery, suggesting early intense bone remodeling that gradually decreases until stabilization at physiologic levels. After 6 months, increased activity was observed

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around intraoral implants following prosthetic restoration.

Bone scintigraphy enables the investigation of bone metabolism in peri-implant zones, providing not only anatomic images, but also information related to physiology and dynamic changes that occur during osseointegration.[2] SPECT methods in particular offer the possibility to reconstruct 3-dimensional (3D) images with the distribution of a radiopharmaceutical that is then taken up by selected bone structures; however, the procedure must be associated with traditional-type radiologic procedures to provide exact data about implant prognosis.[2]

Schliephake and Berding evaluated the bone healing process of autologous onlay grafts in grossly atrophic edentulous jaws in conjunction with delayed placement of endosseous implants using SPECT on 24 patients.[9] A nuclear medicine examination was performed after the intravenous injection of 8 MBq 99mTc–methylene diphosphonate (MDP) per kilogram body weight for each patient immediately after surgery, before implant placement, after implant placement, and before abutment connection. Reference regions of interest (ROIs) were placed over the calvarium to assess semiquantitatively radiotracer distribution by comparing ratios of count densities (counts/pixel) between grafting site ROIs and reference ROIs. The authors demonstrated that bone scintigraphic imaging could be useful for assessing tissue and cellular response and viability of autografts.

In the study by Schliephake and Berding, scintigrams were displayed with a spatial resolution of 15 mm.[9] The latest gamma cameras have been totally digitalized and are equipped with high-resolution collimators that provide a spatial resolution of approximately 7 mm at a distance of 5 cm from the surface of the collimator.[12] The use of the collimator reduces the resolution and the sensitivity of the technique; this fact, associated with the low dose of radiation administered to the patients, seems to produce images that are apparently worse than those created with other diagnostic techniques. In reality, the effectiveness of the image for clinical practice depends on the kind of information that is produced. Large areas of tracer iper-accumulation that identify a neoplasia in the bone are often totally negative for a whole-body, computed tomography (CT) investigation. Thus, there is not any correlation between radiographic and gamma-ray techniques as regards the size and meaning of the images.[12]

Khan and coworkers analyzed the predictability of SPECT methodology in the evaluation of the osseointegration of dental implants.[5] They placed implants in the edentulous jaws of 5 patients and performed SPECT before prosthetic restoration and at regular intervals up to 5 months after loading. Peri-implant osteoblastic activity was compared with activity of ROIs placed within the skull as a reference, so the authors distinguished various phases: *(1)* a rise in cellular activity in the immediate postoperative period; *(2)* a peak of activity that registered 30 days after implant placement, which indicated a bone remodeling process in its maximum productive expression; and *(3)* a gradual decrease in the activity, which returned to normal physiologic levels after 4 months (ie, presurgery levels). The authors stressed the advantages of employing SPECT procedures in implant dentistry and confirmed their usefulness in monitoring the trophic degree of bone when grafting techniques or other surgical procedures are involved.

The aim of the present paper was to evaluate the possibility of performing bone scintigraphy with static acquisitions—both tomographic, through the application of SPECT methods, and planar conventional—to assess the probable influence of immediate functional loading on peri-implant osteoblastic cell activity.

MATERIALS AND METHODS

Two female patients in good health were selected to participate.

In patient A (31 years old), 2 Brånemark System implants (Nobel Biocare, Göteborg, Sweden) were placed in the mandible, in both second premolar edentulous areas. They were MK IV screw-type implants with a machined surface, 10 mm long and 4 mm in diameter. At 48 hours after surgery, a preformed abutment was connected to the implant placed in the right mandibular site and a provisional resin prosthesis was placed (A/1 area, test). The implant placed in the left site was left to heal submerged and later loaded according to standard protocol, so it was used as a control site (A/2 area, control).

In patient B (25 years old), 2 Sudimplant T.B.R.-type implants (Toulouse, France) were placed in the mandible, in both second premolar edentulous areas. These were 10.5 mm long and 4 mm in diameter with a negative surface obtained by removal through sandblasting and acid-etching. After 48 hours, a preformed abutment was placed in the right mandibular site (B/1 area, test) and subjected to functional loading through a resin provisional prosthesis; the implant placed in the left site was left unloaded and used as a control site (B/2 area, control).

At 30 days after implant placement, both patients underwent the first nuclear medicine investigation

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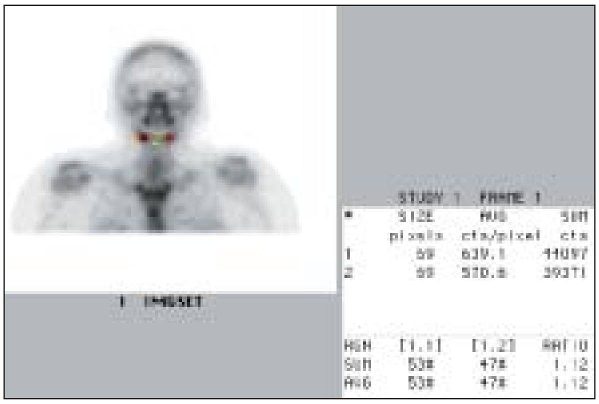

Fig 1a Planar image of patient A performed at 30 days. ROIs and their count density ratios are evident.

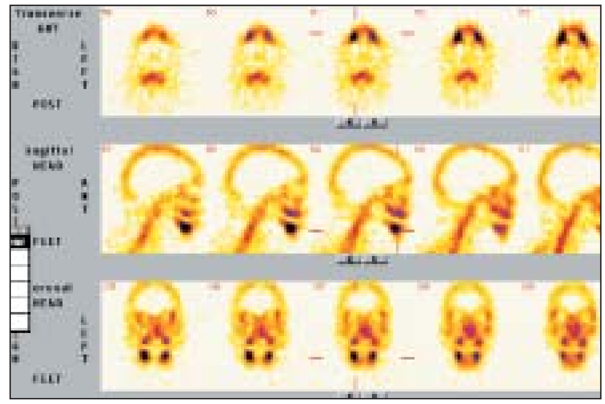

Fig 1b Tomographic images of patient A performed at 30 days, shown on the 3 orthogonal planes.

Table 1 Count Density Ratios (Counts/Pixel) in Test and Control Areas of Both Patients at 30 and 90 Days

	Patient A			Patient B		
Time	Test	Control	Test–control	Test	Control	Test–control
30 days	421.6	505.8	–84.2	639.1	570.6	68.5
90 days	126.4	141.5	–15.1	211.8	227.6	–15.8
30–90 days	295.2	364.3	–69.1	427.3	343.0	84.3

with SPECT and planar conventional methodology. The same investigations were repeated at 90 days. Bone scintigraphy was performed 3 hours after intravenous injection of 740 MBq of 99mTc-MDP, through a double-head rotating Siemens Multispect 2 gamma camera (Erlangen, Germany) with a low-energy/high-resolution collimator (Lehr; Siemens). Specifically, 64 projections were acquired over 360 degrees with a noncircular orbit in a 128×128 matrix through a "steep and shoot" modality with an angular interval of 5.6 degrees. Standard software for data re-elaboration was used (Icon-Siemens Gammasonics, Erlangen, Germany). Tomographic images were elaborated through a retro-projection algorithm using a Butterworth filter, cutoff frequency 0.6, and order number 10 and reconstructed according to the 3 orthogonal planes of the space: transverse, sagittal, and coronal. The study was completed with planar conventional acquisitions of the skull in an anterior view, with placement of ROIs of the same size on the areas corresponding to the test and control sites in the opposite hemimandible.

Drawings of the ROIs (size and location) were made by hand on the monitor display around the areas of tracer iper-accumulation with special care to ensure that the test and control drawings for each patient were identical in size. The difference of a few pixels in the size of the ROIs between the 2 patients was not considered significant because a direct comparison was not made between them.

Ratios of count densities (counts/pixel) obtained from each ROI were used for a quantitative-relative evaluation. The tomographic images were investigated with a qualitative method. In this study, scintigrams were displayed with a spatial resolution of 15 mm.

RESULTS

During the weeks following implant surgery, no complications occurred and normal healing was observed in both patients. No ratios of count densities were carried out from tomographic images, as they were used for a qualitative study.

From planar images acquired after 30 days, the authors obtained the following values after ROI placement:

- For patient A, 2 ROIs of 68 pixels each were placed. This provided 28,670 counts from the test area (A/1) with a ratio of 421.6 counts/pixel and 34,393 counts from the control area (A/2) with a ratio of 505.8 counts/pixel (Figs 1a and 1b; Table 1).
- For patient B, 2 ROIs of 69 pixels each were placed. This provided 44,097 counts from the test area (B/1) with a ratio of 639.1 counts/pixel and 39,371 counts from the control area (B/2) with a ratio of 570.6 counts/pixel (Figs 2a and 2b).

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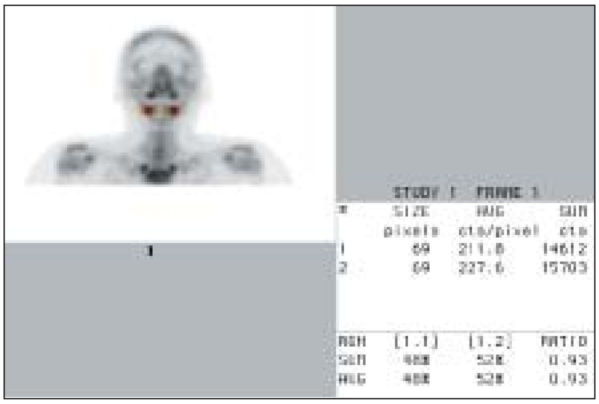

Fig 2a Planar image of patient B performed at 30 days. ROIs and their count density ratios are evident.

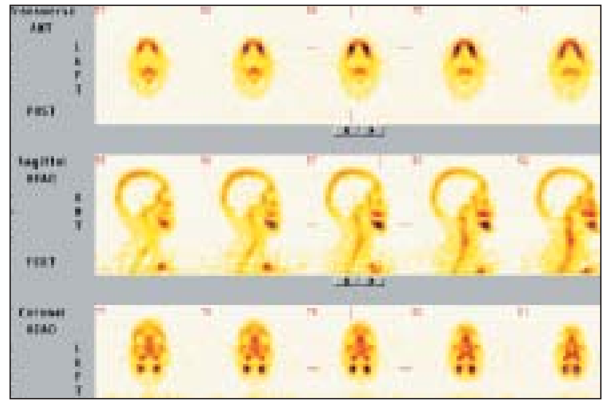

Fig 2b Tomographic images of patient B performed at 30 days, shown on the 3 orthogonal planes.

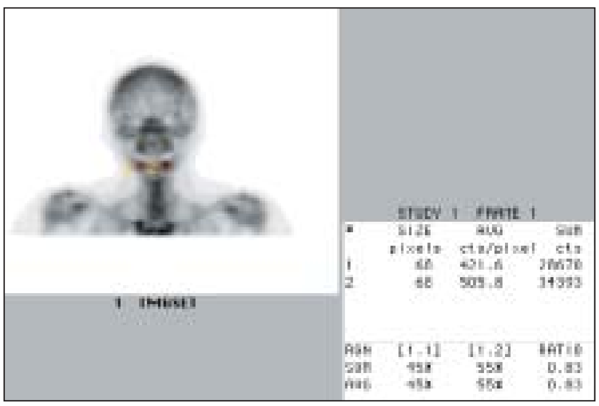

Fig 3a Planar image of patient A performed at 90 days. ROIs and their count density ratios are evident.

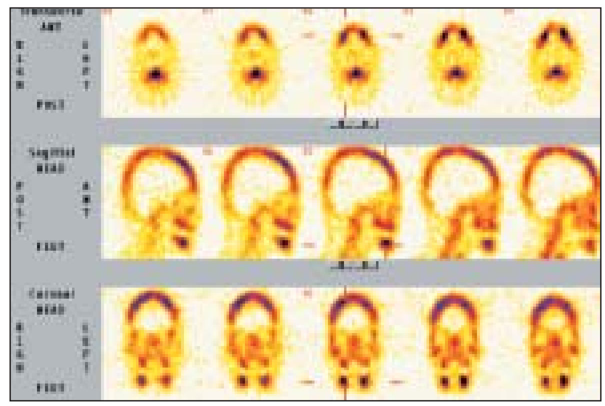

Fig 3b Tomographic images of patient A performed at 90 days, shown on the 3 orthogonal planes.

The same process was repeated 90 days after surgery with the following results:

- For patient A, 2 ROIs of 74 pixels each were placed. This provided 9,352 counts from the test area (A/1) with a ratio of 126.4 counts/pixel and 10,474 counts from the control area (A/2) with a ratio of 141.5 counts/pixel (Figs 3a and 3b).
- For patient B, 2 ROIs of 69 pixels each were placed. This provided 14,612 counts from the test area (B/1) with a ratio of 211.8 counts/pixel and 15,703 counts from the control area (B/2) with a ratio of 227.6 counts/pixel (Figs 4a and 4b).

Conventional radiologic images of both patients confirmed the success of implant placement (Figs 5a and 5b).

DISCUSSION

Regarding patient A, from the data relative to bone scintigraphy performed at 30 days, the count density ratio was higher in the control area (A/2) than in the test area (A/1), with a difference of 5,723 counts, which was equivalent to 84.2 counts/pixel. Data referred to bone scintigraphy performed at 90 days gave a higher count density ratio in A/2 than in A/1, this time with a difference of 1,122 counts, which was equivalent to 15.1 counts/pixel.

The first finding evolving from this study was the higher cellular activity registered in the control area (delayed loading) than in the test area (immediate loading), at both 30 and 90 days. The second factor was the difference in counts registered from the same ROI between the first and the second scintigraphic studies. The authors assessed 295.2 counts/pixel for the test area (A/1) and 364.3 counts/pixel for the control area (A/2). This information suggested that during the osseointegration process, after the first month, osteoblastic peri-implant activity was very high and then declined rapidly during the few following months. There was also a difference in the decrease gradients of cellular activity referred to the 2 areas (test and control), although these differences were not statistically significant because of the small

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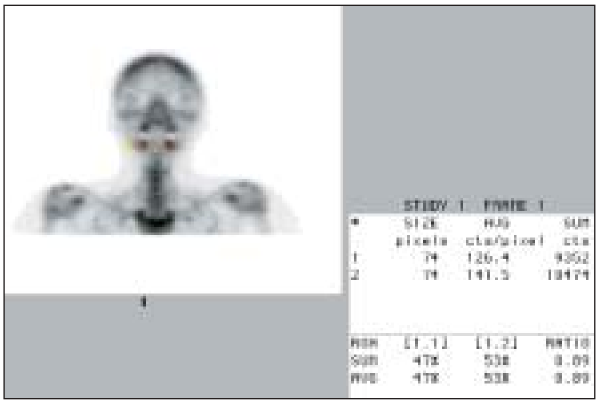

Fig 4a Planar image of patient B performed at 90 days. ROIs and their count density ratios are evident.

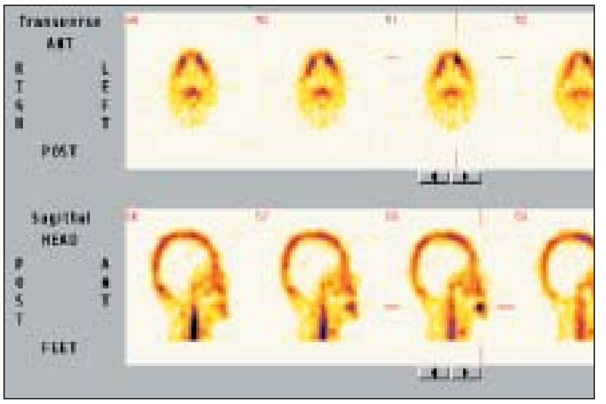

Fig 4b Tomographic images of patient B performed at 90 days, showed on the three orthogonal planes.

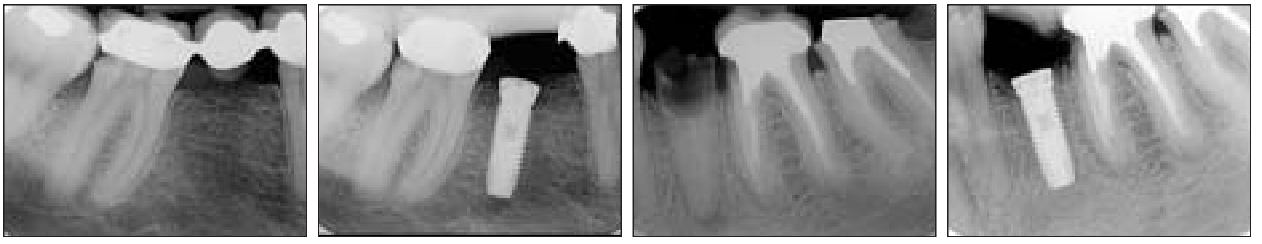

Fig 5a Conventional radiologic images of patient A performed before and after implant placement.

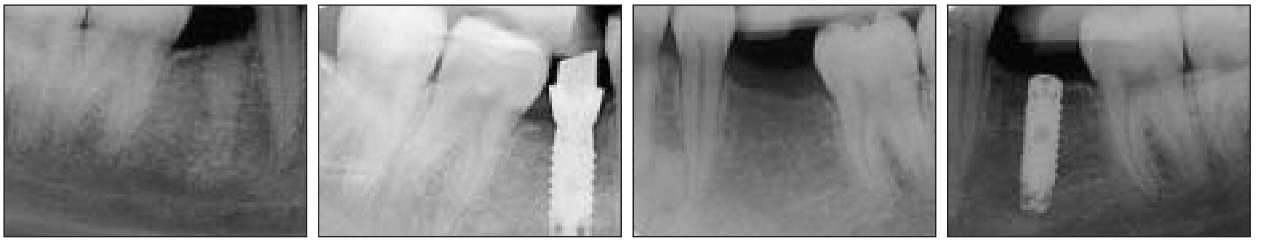

Fig 5b Conventional radiologic images of patient B performed before and after implant placement.

number of involved cases and the lack of absolute reference values.

Regarding patient B's results, from re-elaboration of the data obtained from the planar conventional images performed at 30 days, the count density ratio was lower in the control area (B/2) than in the test area (B/1), with a difference of 4,726 counts, equivalent to 68.5 counts/pixel. The values relative to the examination repeated at 90 days underlined an inversion of tendency, with a count density ratio that was higher in area B/2 than in area B/1, with a difference of 1,091 counts, equivalent to 15.8 counts/pixel. These data may suggest that whereas at 30 days a higher cellular peri-implant activity was observed around the immediately loaded implant (area B/1) than around the control implant, at 90 days the opposite situation appeared, with osteoblastic activity more evident at the control site. Regarding the difference in count density ratios registered from the same ROI between the first and the second nuclear medicine examination for patient B, there was an analogous situation to patient A, both in the test area (B/1), where there was a difference of 427.3 counts/pixel, and in the control area (B/2), where there was a difference of 343 counts/pixel. The data indicate how cellular activity, which was very high in both areas after 1 month from the surgery, had collapsed by 90 days. It was impossible to establish the statistical importance of the difference between the decrease gradients of osteoblastic activity in the 2 areas (test and control), for the aforementioned reasons.

In spite of the small number of patients involved, the results obtained from this pilot study prompt some important considerations. Osseointegration is a process that involves implant anchorage in bone

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through direct tissue-to-titanium contact, as reported by Albrektsson and Johansson.[13] This process starts during the surgery in which the implant site is prepared, because the surgical act presents the same biologic characteristics as a fracture and permits immature bone cells to explicate their natural osteoinductive potential as soon as the bone is damaged. This process peaks in intensity during the first month and then gradually decreases up to the fourth month, according to some authors[2,5] and the present results.

Immediate loading showed positive results for the osseous reparative and integrative mechanism in patient B. The surface seemed to play an important role in the osseous integrative process, as if the rugophilic properties of osteoblasts—as in the recently reported high success rates of rough titanium implants by several authors[14–18]—were shown to their full advantage in immediate loading, according to values registered for the patient with sandblasted/acid-etched implants. Jaffin and coworkers[19] and Roccuzzo and associates[20] stressed the advantages of sandblasted/acid-etched implant surfaces used, respectively, in immediate and early loading procedures.

Nuclear medicine investigations provide images and measures of the distribution of a radiotracer that is accumulated and metabolized by tissues and organs; they give information about the level of activity of these structures. Unfortunately, clinical diagnoses cannot be made from these exams.

In bone scintigraphy, diphosphonates are currently used as radiotracers. The diphosphonates link themselves to the newly produced bone matrix before thorough absorption, then to the crystalline reticule and to the matrix itself. This technique can reveal every type of osteoblastic activity, providing information concerning primary tumors, osteomyelitis, fractures, metastases, Perthes disease, bone metabolic disease, and Paget disease, and can investigate bone pain.[12] The bone scintigraphy is negative for all of these osteolithic pathologies because 99mTc-MDP does not come into the osteoclast metabolic cycle.[12] Bone captation is about 70% of the administered dose during skeletal scintigraphy, so the radiotracer is selective enough in comparison with radiographs, which penetrate all the tissues in a predetermined area.[21,22]

The radiation dose absorbed by bone tissue is 9.5 μGy/MBq (7.03 mGy for 740 MBq of 99mTc-MDP), which is lower than that absorbed by eye, thyroid, and bone marrow during a CT investigation of the head (25 scansions), an examination that is often required by clinicians before implant placement.[21,22] Bone scintigraphy and, more generally, nuclear medicine investigation do not involve high costs of maintenance comparable to other diagnostic machines, such as CT and magnetic resonance imaging. Moreover, any gamma camera can be used for a particular technique or instrument required for an oral cavity investigation.

Nuclear medicine offers the clinician great diagnostic potential in bone pathology, because a metastatic lesion can be revealed through areas of increased fixation many months before the bone erosion gives any radiologic sign of the pathology.[12]

SUMMARY

Studies dealing with immediate loading protocols are needed to provide exact and potentially encouraging data regarding the possibility for accelerating the healing time of endosseous implants. The present results suggest that bone scintigraphy and SPECT can represent a valid instrument for monitoring bone healing in immediate loading procedures.

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