Comparison of Radiographic Appearance and Bone Scintigraphy in Fracture Nonunions

TAKAHIRO NIIKURA, MD; SANG YANG LEE, MD; YOSHITADA SAKAI, MD; KOTARO NISHIDA, MD; RYOSUKE KURODA, MD; MASAHIRO KUROSAKA, MD

abstract

Many surgeons assess the biological activity of fracture nonunions by the presence or absence of callus on radiographs. However, the assessment of biological activity by radiographic appearance alone is controversial. Bone scintigraphy reflects blood flow and new bone formation; therefore, it is useful in assessing such biological activity in nonunion cases. This retrospective study compared radiographs with Tc-99m bone scintigraphy in 48 patients with uninfected nonunions. Positive uptake was observed in all cases. The uptake patterns were classified into 4 types: type 1, intense, uniform uptake; type 2A, a definite photon-deficient cleft between 2 areas of intense uptake; type 2B, a photon-deficient area other than type 2A; and type 3, an intermediate pattern with uneven, distributed uptake. The percentage of type 1 with intense uptake does not decrease with time, and type 2 does not increase. When uptake was compared in patients with a nonunion and a united fracture, higher uptake in nonunion was seen in 46% and lower uptake was seen in 27%. All cases of hypertrophic and more than half of oligotrophic nonunions were type 1. Type 2 was seen in 17% of oligotrophic, 67% of comminuted, 100% of defect, and 57% of atrophic nonunions. Poor callus visualization may not preclude biological activity. Long duration from injury may not equate to declines in biological activity. Comparing uptake in nonunions and united fractures in the same patient may help to assess biological activity. The photon-deficient area is helpful to assess the necessity of bone graft or other osteogenic supplementation.
Five to 10% of fractures are estimated to result in nonunion or delayed union, and they present challenges for surgeons. To treat a nonunion, it is important to assess whether the nonunion site is biologically active. If the nonunion shows a lack of biological activity, surgeons need to supplement some biological activity.

Many surgeons assess the biological activity of nonunions by the presence or absence of callus on radiographs. The presence of callus formation is usually assessed as the presence of biological activity, and the absence or paucity of callus formation is usually assessed as the absence or paucity of biological activity by radiographic appearance. However, assessing biological activity only by radiographic appearance is controversial. Poor callus visualization on radiographs may be due to not only poor biological activity but also inadequate fracture management, including reduction and fixation. In addition, the terms hypertrophic and atrophic are based on radiographic appearance.

Bone scintigraphy with technetium (Tc)-99m-labeled diphosphonates is one of the most frequently performed radionuclide procedures. It is quick, relatively inexpensive, widely available, and sensitive. The degree of radiotracer uptake depends primarily on 2 factors: blood flow and new bone formation. Because bone scintigraphy reflects the combination of blood flow and new bone formation, it is useful in assessing biological activity in nonunion cases. It was reported that uptake was observed in nonunion cases and bone scintigraphy allowed early detection of a pathological course of fracture healing. In addition, uptake in bone scintigraphy was reported to be an important indicator predicting the effectiveness of electric stimulation or extracorporeal shock wave. However, more detailed information about the pattern and feature of uptake in nonunions is needed, and to the current authors’ knowledge, there are no detailed reports comparing radiographic appearance with bone scintigraphy. Therefore, the purpose of this study was to investigate the detailed pattern and features of uptake and perform a comparison of radiographic appearance and bone scintigraphy in fracture nonunions.

**Materials and Methods**

Retrospective assessment was performed of radiography and bone scintigraphy of 48 consecutive patients treated for uninfected nonunion at the authors’ hospital from July 2008 onward. The hospital’s ethics committee approved the study.

Patient characteristics and clinical results were investigated by reviewing medical charts. Thirty-six males and 12 females were included, with an average age of 50.3 years (range, 13-82 years). Fractures included 5 clavicle, 4 humerus, 1 radius, 16 femur, 21 tibia, and 1 fibula. Ten patients were treated conservatively, and 38 had undergone previous surgery. Fixation devices applied at the time of the bone scintigraphy were intramedullary nails (n=21), plates (n=12), and external fixators (n=4). One patient with a fibular nonunion was treated by percutaneous drilling and no internal fixation. There were 5 synovial pseudoarthroses with massive abnormal mobility, such as a joint and synovial fluid collection in the pseudocapsule confirmed at surgery. Mean duration from injury to nonunion surgery was 22.0 months (range, 5-128 months). Fixation devices were used in 34 patients, and all patients achieved bony union and regained function of the extremities.

Radiographs were reviewed to classify the nonunions according to radiographic criteria and assessing bony union after treatment. The nonunions were classified into the hypertrophic type (elephant foot and horse hoof), oligotrophic type, comminuted type (torsion-wedge, dystrophic, and necrotic), defect type, and atrophic type. Synovial pseudoarthrosis and nonunion were assessed separately with the idea that these are 2 distinct pathologic entities.

Bone scintigraphy performed before nonunion surgery was reviewed. Bone scintigraphy was performed 3 hours after intravenous injection of Tc-99m hydroxy methylene diphosphonate or Tc-99m methylene diphosphonate. At least 4 views were obtained. The intensity of uptake was visually assessed using a grading system: cold uptake (less than the contralateral bone), faint uptake (equal to the contralateral bone), moderate uptake (more than the contralateral bone but less than the contralateral epiphyseal or vertebral endplate uptake), and high uptake (equal to or more than the contralateral epiphyseal or vertebral endplate uptake).

**Results**

According to radiological classification, nonunions were classified as follows: 7 hypertrophic, 18 oligotrophic, 6 comminuted, 5 defect, and 7 atrophic. There were 5 synovial pseudoarthroses.

On bone scintigraphy, positive uptake was observed in all cases. Uptake patterns were classified as follows: type 1, a photon-deficient area was absent, and intense, uniform uptake was observed; type 2A, a definite photon-deficient cleft was present between 2 intense areas of uptake; type 2B, a photon-deficient area was present other than type 2A; and type 3, uneven, distributed uptake was observed without evidence of a photon-deficient area. Overall, 44% of observed uptake patterns were type 1, 21% were type 2A, 14% were type 2B, and 21% were type 3 (Figure 1).

Uptake was observed in 2 patients more than 100 months after injury. Patients were divided according to duration from injury: less than 12 months (n=19), between 12 and 24 months (n=17), and 24 or more months (n=12). The percentage of type 1 with intense uptake did not decrease, and type 2 with a photon-deficient area did not increase with the increase of duration from injury (Table 1).

Uptake in nonunions was compared with united fractures in the same patients (15 patients). In this investigation,
fibula fractures accompanied by tibial nonunions were excluded. Higher uptake in nonunions compared with united fractures was observed in 46%, same-grade uptake in 27%, and lower uptake in 27% (Figure 2A). In addition, uptake in tibial nonunions (9 patients) was compared with accompanied fibula fractures that united. Uptake was higher in 89% of tibial nonunions, and 11% showed same-grade uptake (Figure 2B).

All 7 cases of hypertrophic nonunion were type 1. In 18 cases of oligotrophic nonunion, there were 10 cases of type 1, two cases of type 2A, 1 case of type 2B, and 5 cases of type 3. In 6 cases of comminuted nonunion, there were no cases of type 1, one case of type 2A, 3 cases of type 2B, and 2 cases of type 3. In 5 cases of defect nonunion, there were no cases of type 1, two cases of type 2A, 3 cases of type 2B, and no cases of type 3. In 7 cases of atrophic nonunion, there were no cases of type 1, four cases of type 2A, 0 cases of type 2B, and 3 cases of type 3. In 5 cases of synovial pseudoarthrosis, there were 4 cases of type 1, one case of type 2A, and 0 cases of types 2B or 3 (Table 2).

Furthermore, the percentage of type 2 with a photon-deficient area was investigated. No hypertrophic, 17% of oligotrophic, 67% of comminuted, 100% of defect, and 57% of atrophic nonunions and 20% of synovial pseudoarthroses demonstrated a photon-deficient area (Table 3).

CASE REPORTS

Patient 1

A 57-year-old man’s tibial shaft fracture was treated with an intramedullary nail. Thirteen months later, radiography showed hypertrophic nonunion, and bone scintigraphy showed type 1 uptake. Exchange nailing was performed, and bony union was obtained (Figure 3).

Patient 2

A 76-year-old woman’s distal tibial and fibular fractures were treated with a locking plate. The tibial fracture was a type IIIA open fracture according to Gustilo-Anderson classification, and the ends of the bony fragments were exposed outside the skin. Seven months later, radiography showed atrophic nonunion, and bone scintigraphy showed type 2A uptake. Ilizarov external fixation and autologous bone grafting were performed, and bony union was obtained (Figure 4).

Patient 3

A 23-year-old man’s tibial shaft comminuted fracture was treated with an intramedullary nail. Twenty months later, this case accompanied valgus deformity. Radiography showed comminuted nonunion, and bone scintigraphy showed type 2B uptake. Deformity correction, locking plate fixation, and autologous bone graft-
ing were performed, and bony union was obtained (Figure 5).

**Patient 4**

A 34-year-old man’s distal femoral comminuted fracture was treated with a locking plate. Nine months later, this case accompanied implant breakage. Radiography showed comminuted nonunion, and bone scintigraphy showed type 3 uptake. An accompanying patellar fracture showed intense uptake. Revision of locking screws and autologous bone grafting were performed, and bony union was obtained (Figure 6).

**Patient 5**

A 45-year-old man sustained a right femoral shaft fracture, left tibial plateau fracture, and left tibial shaft fracture. The right femoral shaft fracture and left tibial plateau fracture healed uneventfully, but the left tibial shaft fracture did not heal 6 months after injury. In this patient, the uptake of the nonunion was higher than that of the united fractures (Figure 7).

**Discussion**

Desai et al., Esterhai et al., and Heppenstall et al. reported a similar classification of uptake in nonunions. The difference between their classifications and the current classification is that the current authors classified a photon-deficient type in detail. The authors found that a photon-deficient area was not always a definite linear cleft and added a new type. In addition, the aforementioned studies used bone scintigraphy mainly for detection of synovial pseudoarthrosis because they believed that electric stimulation was not effective for synovial pseudoarthrosis differing from nonunion. They reported that a photon-deficient cleft is an important finding to detect synovial pseudoarthrosis. However, the current authors experienced synovial pseudoarthrosis cases with intense, uniform uptake without cleft visualization. If the space of the pseudocapsule is narrow, a photon-deficient cleft may not be seen. If

<table>
<thead>
<tr>
<th>Variable</th>
<th>Photon-deficient Area, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonunion</td>
<td></td>
</tr>
<tr>
<td>Hypertrophic</td>
<td>0</td>
</tr>
<tr>
<td>Oligotrophic</td>
<td>17</td>
</tr>
<tr>
<td>Comminuted Defect</td>
<td>67</td>
</tr>
<tr>
<td>Defect</td>
<td>100</td>
</tr>
<tr>
<td>Atrophic</td>
<td>57</td>
</tr>
<tr>
<td>Synovial pseudoarthrosis</td>
<td>20</td>
</tr>
</tbody>
</table>

Table 3

Nonunions and Synovial Pseudoarthroses With a Photon-Deficient Area

Figure 3: Radiograph of patient 1 showing hypertrophic nonunion (A) and bone scintigraphy showing type 1 uptake (B).

Figure 4: Radiograph of patient 2 showing atrophic nonunion (A) and bone scintigraphy showing type 2A uptake (B).

Figure 5: Radiograph of patient 3 showing comminuted nonunion (A) and bone scintigraphy showing type 2B uptake (B).

Figure 6: Radiograph of patient 4 showing comminuted nonunion (A) and bone scintigraphy showing type 3 uptake (B).

Figure 7: Radiograph of patient 5 showing intense, uniform uptake without cleft visualization (A) and bone scintigraphy showing type 4 uptake (B).
the uptake to the bone fragments facing each other is intense, the photon-deficient cleft may be hidden. Furthermore, the aforementioned studies\textsuperscript{12,13,15,17} did not compare the uptake pattern with radiographic appearance. The current authors investigated the features and patterns of uptake of not only synovial pseudoarthroses but also nonunions in more detail.

A radiographic appearance of hypertrophic nonunion is generally recognized as a nonunion-preserving biological activity.\textsuperscript{3-5} In the current study, all hypertrophic nonunion cases demonstrated intense, uniform uptake in bone scintigraphy. This result agrees with the general consensus regarding biological activity of hypertrophic nonunion. The uptake pattern of the comminuted type and defect type of nonunion has not been fully reported. A photon-deficient area and uneven uptake were observed in comminuted type and defect type nonunions in this study. The authors suggested that this uptake pattern reflects the comminution and bony defect at the fracture site. It is recognized that there are nonunions with decreased biological activity in these types of nonunions. The uptake pattern of oligotrophic nonunion, which also shows poor or absent callus formation, is notable. Of these, 56% demonstrated intense, uniform uptake and only 17% demonstrated a photon-deficient area. The authors’ results suggest that poor or absent callus visualization on radiographs does not always mean a lack of biological activity.

In this study, uptake was observed in all cases. Seventy-seven percent (37 of 48) of cases were implanted with metal fixation devices. A bone scintigraph could be obtained even in cases with metal implants. The authors believe that bone scintigraphy is useful to assess whether additional stabilization is sufficient or whether adding biological activity, such as autologous bone grafting, is needed in nonunion surgery. The photon-deficient area is helpful in determining the necessity of a bone graft or other supplementation, such as bone morphogenetic proteins, in nonunion surgery.

The meaning of the photon-deficient area warrants further discussion. Many atrophic nonunions demonstrated a photon-deficient cleft, and even the cleft showed faint uptake. This raises the question of whether the decrease in uptake indicates a decrease in blood flow, new bone formation, or both as reflected by bone scintigraphy. Reed et al\textsuperscript{19} reported that atrophic nonunions were not avascular by a histological investigation of biopsied human nonunion tissue. Garcia et al\textsuperscript{20} reported that in atrophic nonunions, the expression of vascular endothelial growth factor, which is an important inducer of angiogenesis, was not reduced, and the expression of bone morphogenetic protein, which is an osteogenic mediator, was reduced compared with united fractures in an animal study. The current authors considered that blood supply was preserved but osteogenic activity was decreased at the photon-deficient area; therefore, the supplementation of osteogenic activity was necessary and appropriate for the treatment approach in atrophic nonunions.

Figure 7: Case 5: 45-year-old man. Right femoral shaft fracture (A) and left tibial plateau fracture (B) healed uneventfully, but left tibial shaft fracture (B) did not heal 6 months after the injury. The uptake of nonunion is higher than united fractures (C).
To the authors’ knowledge, there are no detailed reports describing how long uptake can be observed in nonunion cases. The authors detected clear uptake in a patient whose fracture was older than 10 years. This suggests that some biological activity is present even 10 years after fracture. The percentage of intense, uniform uptake did not decrease, and uptake with a photon-deficient area did not increase with the increase in duration from injury. It is a useful reminder that a long duration from fracture does not always mean a loss of biological activity.

In this study, the authors performed the first comparison of uptake in a nonunion and a united fracture in the same patient and of uptake in tibial nonunions and accompanying fibular fractures. These comparisons may help to assess pathological condition and biological activity.

The authors found a correlation between the surgical findings and the photon-deficient findings on bone scintigraphy. Nonhypertrophic nonunions with photon-deficient areas on bone scintigraphy demonstrated bone-deficient areas induced by comminution, gaps, or bone defects on surgical findings. Fibrous tissue formed at the bone-deficient area. Therefore, these findings suggest that the fibrous tissue formed at the bone-deficient area is deficient in biological activity. The authors suggest that the deficiency of biological activity comprises a deficiency of both blood flow and osteogenic activity because little bleeding from the fibrous tissue was detected when it was excised. They believe that the degree of photon deficiency seen on bone scintigraphy correlates with the extent of the bone-deficient area.

Although bone scintigraphy is useful in assessing biological activity, there are some limitations to this approach. Uptake in bone scintigraphy reflects blood flow and new bone formation; however, it is difficult to know the ratio of these 2 factors. In addition, the presence of biological activity can be established if uptake is observed; therefore, qualitative assessment can be performed. However, quantitative assessment is difficult. This limitation should be considered when bone scintigraphy is used for the assessment of biological activity in fracture nonunion cases.

The authors would like to expand the possible clinical applications of this study. The authors tried to establish a treatment algorithm of uninfected nonunions, including the necessity of bone scintigraphy (Figure 8). At first, hypertrophic nonunions do not need bone scintigraphy, and secure fixation will lead to bony union. The authors recommend that bone scintigraphy be performed for nonhypertrophic nonunions. If a photon-deficient area is detected on bone scintigraphy, then an autologous bone graft can be supplemented. Other osteogenic supplementations, such as bone morphogenetic protein, are optional. If a photon-deficient area is not detected, then secure fixation is sufficient to achieve bony union.

**Conclusion**

Bone scintigraphy is useful in assessing biological activity in fracture nonunions in addition to radiographic assessment.

**References**

15. Esterhai JL Jr, Brighton CT, Heppenstall

---

**Figure 8**: Treatment algorithm showing the necessity of bone scintigraphy for uninfected nonunions.


