SCIENTIFIC ARTICLE

Quantitative assessment of mineralization in distraction osteogenesis

Sunit Hazra · Hae-Ryong Song · Sandeep Biswal · Suk-Ha Lee · Seok Hyun Lee · Ki-Mo Jang · Hitesh N. Modi

Abstract

Objectives The most important decision in distraction osteogenesis is the timing of fixator removal. Various methods have been tried, such as radiographic appearance of callus and bone mineral density (BMD) assessment, but none has acquired gold standard status. The purpose of this study was to develop another objective method of assessment of callus stiffness to help clinicians in taking the most important decision of when to remove the fixator.

Materials and methods We made a retrospective study of 70 patients to compare the BMD ratio and pixel value ratio. These ratios were calculated at the time of fixator removal, and Pearson's coefficient of correlation was used to show the comparability. Inter- and intra-observer variability of the new method was also tested.

Results Good correlation was found between BMD ratio and pixel value ratio, with a Pearson's coefficient of correlation of 0.79. The interobserver variability was also low, with high intra-observer reproducibility, suggesting that this test was simple to perform.

Conclusion Pixel value ratio is a good method for assessing callus stiffness, and it can be used to judge the timing of fixator removal.

Keywords Distraction osteogenesis · BMD · Callus stiffness · Pixel · Lengthening · Ilizarov

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Introduction

The most critical decision in the process of distraction osteogenesis (DO) is when to remove the external fixator. Standard radiography in two planes, together with the surgeon's clinical judgment, remains the main tool in clinical practice [1, 2]. Traditional radiographic techniques only allow qualitative assessment of new bone formation, thus providing limited guidance in deciding when to discontinue use of the fixator [3]. Quantitative methods include quantitative computer tomography [4], quantitative technetium scintigraphy [5] and dual-energy X-ray absorptiometry (DEXA) [6–8]. These methods measure callus mineralization, which has been found to correlate well with callus stiffness [9]. DEXA is most commonly used for assessment of callus bone mineral content (BMC) and bone mineral density (BMD).

The picture archiving communication system (PACS) is increasingly being used for the assessment of medical images [10]. We hypothesized that the pixel value of any

point in radiographs, measured with the pixel lens in the tools palette, would provide an objective value for measurement of callus stiffness. The pixel value in PACS is calculated by the following formula:

$$Q = Q0 + 1024/(L \times [\mu1\,T1 + \mu2\,T2]),$$

where Q=pixel value of the region of interest; Q0=pixel value of background; L=latitude value of imaging plate; μl= linear attenuation coefficient of bony tissue (per centimeter); T1=thickness of bony tissue (in centimeters); μ2=linear attenuation coefficient of soft tissue (per centimeter); and T2=thickness of soft tissue [14].

The purpose of this study was to validate pixel ratio measurement of the callus by comparing it with an established procedure such as DEXA. We also studied its intra-observer reproducibility and interobserver reliability.

Materials and methods

A retrospective analysis of 70 tibial segments in 40 patients was performed. The patients' mean age was 11 years (range 6–22 years). There were 19 male patients and 21 female patients, of whom only five were skeletally mature. Indications for limb lengthening to be performed were achondroplasia in 22 patients, limb length discrepancy in ten patients, and idiopathic short stature in four patients; four patients had other indications. All patients had undergone tibial lengthening by Ilizarov external fixator, operated by a single experienced surgeon (H.R.S.). The mean amount of lengthening was 5.2 cm (range 3.8–10.6 cm). The mean healing time was 34 days (range 22–49 days).

Evaluations

BMD was measured with a Hologic QDR 1000 instrument (Massachusetts, USA). Three regions of interest were evaluated: proximal (from the osteotomy site to the proximal ring), callus, and distal (between the distal ring and the distal osteotomy) (Fig. 1). The BMD ratio was calculated from the ratio of the BMD value of the regeneration area to proximal area. The value of the distal segment was not used, because the latter undergoes severe osteoporosis during lengthening.

Pixel value ratio was measured on standard radiographs with STAR PACS Pi view STAR 5.0.6.1 software (INFINITT Co, LTD, Seoul, Korea). The pixel value was measured with the pixel lens included in the tools of the PACS workstation (Fig. 2a). The pixel value of the regeneration area was calculated from three cortical and three medullary readings each, on both anteroposterior and lateral views. One reading was taken at the center of the callus, and the other two at the midpoint of the center and the osteotomised ends proximally and distally (Fig. 2b). The average of the resulting 18 values (nine values in each of the two views) was used for further evaluations of callus stiffness. For measuring the pixel value of the proximal end, three readings were taken once in each cortex and medulla at the midpoint of the osteotomized end and the proximal ring in both anteroposterior and lateral views (Fig. 2b); care was taken to avoid any metal. The

Fig. 1 Image showing the BMD assessment from different areas. *R1* proximal segment, *R2* callus regenerate area, *R3* distal segment. The chart shows the different values obtained
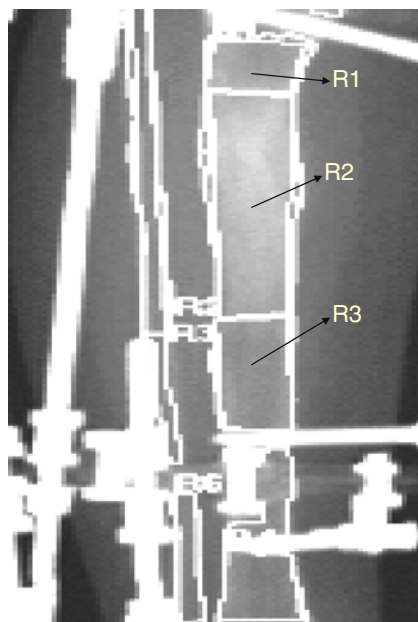
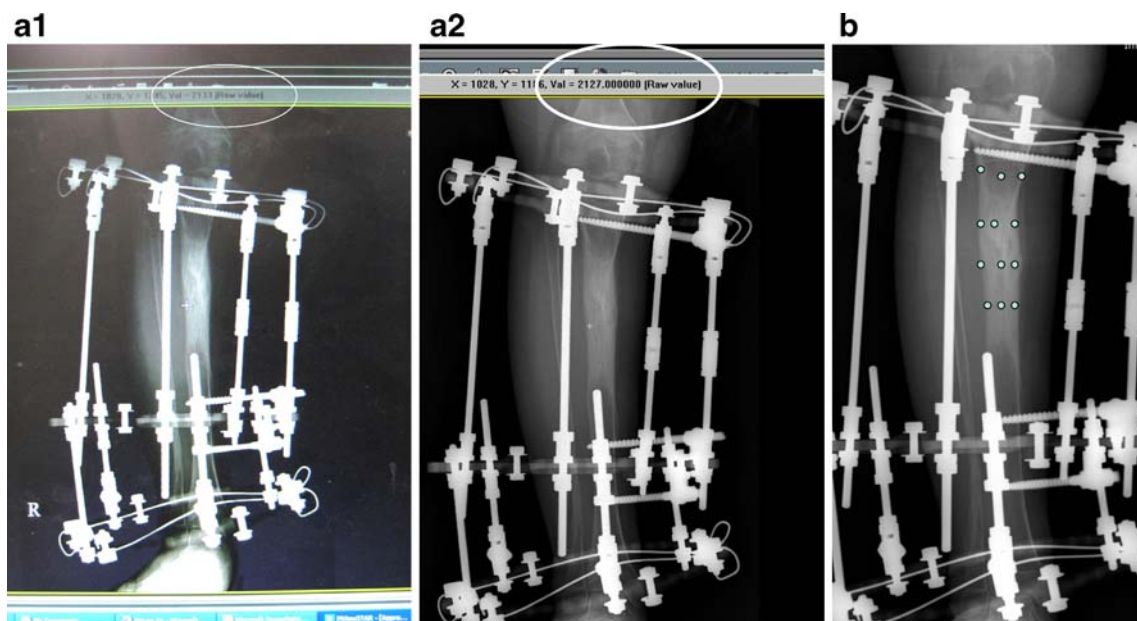| Region	Area(cm²)	BMC(gm)	BMD (gm/cm²)
R1	3.89	2.06	0.531
R2	13.31	10.21	0.767
R3	6.19	2.63	0.426

Fig. 2 a Pixel value assessment from a radiograph in a PACS workstation. Note the *circle* showing the pixel value of that particular point where the marker is positioned. **b** Points marked on the radiographs where pixel values were taken. Note the nine points in the regeneration area and the three points in the proximal segment

mean of the six resulting values was taken as the pixel value of the proximal segment. Since we had measured the raw pixel value, expressed in the monochrome 1 photometric interpretation of the digital imaging communication in medicine (DICOM) protocol, which is inversely related to radiopacity, i.e. with increase in radiopacity the raw pixel value decreases. So we took the inverse ratio, i.e. we took the ratio of the pixel value of the proximal segment to that of the regeneration area.

In order to test interobserver and intra-observer variability of the pixel value ratio, three physicians performed the measurements (one senior pediatric orthopedic surgeon, one pediatric orthopedic fellow and one hip fellow). The radiographs were reviewed twice by each reviewer, with a minimum interval of 2 weeks. The radiographs were presented in different orders for the second reading by shuffling the identification numbers list that was supplied. Prior to embarking on the study the reviewers were provided with a written description of the radiograph assessment,, with special emphasis on the points where the value should be measured. The descriptions were again presented before the second evaluations. There were no time limits. Two radiographs with metal in the vicinity of the region of interest were added purposely, so that it could be determined whether the reviewers had understood the proper method of assessment of the radiographs.

The pixel value ratio and BMD ratio were compared, using a Pearson correlation coefficient. Intra-observer and interobserver variability was also tested with Pearson correlation coefficients.

Results

For BMD ratio and pixel value ratio the Pearson correlation coefficient was 0.79, suggesting good linear correlation between BMD ratio and pixel value ratio. A scatter plot also showed good correlation, with limited variability (Fig. 3).

Intra-observer variability, measured by three different observers at two different timepoints, were 0.91, 0.90 and 0.88; the mean Pearson correlation coefficient was 0.90.

Interobserver variability for each pair of observers (A and B, A and C, B and C) was also measured, during both
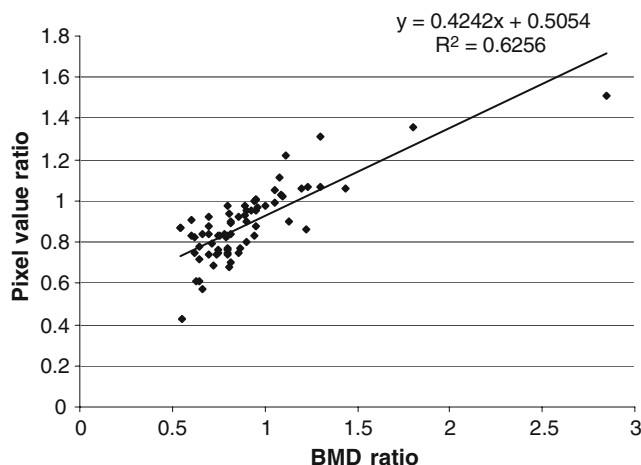

Fig. 3 Linear correlation between BMD ratio (x-axis) and pixel ratio (y-axis)

the first reading and the second reading. The values for the pairs of observers were 0.85, 0.91 and 0.92 during the first evaluation and 0.87, 0.88 and 0.89 during the second evaluation.

Discussion

PACS has made original DICOM data sets widely available [11–14], allowing for hospital-wide electronic measurements, including determination of pixel values, which, in part, depend on the mineral content of bone [15]. Although such pixel values are not absolute values, the relative pixel value ratio can provide information regarding bone healing.

Timing fixator removal in limb lengthening is an important decision. Leaving the frame for longer than necessary would lead to various complications, such as limitation of joint motion due to contracture. However, premature removal of the frame also leads to serious complications, like fracture, and axial bending at the callus. Ilizarov himself remarked that "leaving the apparatus on for longer than necessary is as harmful as removing the fixator too early" [16]. Most clinicians take this vital decision on the basis of their clinical experience and the radiographic appearance of the callus [1, 2]. Fischgrund et al. [17] specified the presence of three of the four cortices of a minimum 2 mm thickness as a guideline for removal of the fixator. They presented a re-fracture rate of only 3%. However, this method did not provide good intra-observer and interobserver reproducibilities, as tested by Starr et al. [18]. They attributed the good results obtained by Fischgrund et al. [17] to better clinical judgment of an experienced surgeon involved in decision making, rather than the radiographic criteria demonstrated in their study [18]. The other method that has been used for assessing callus stiffness is measurement of BMD [6–8], which has been proven to represent callus strength [9]. DEXA is most commonly used for the evaluation of BMD. However, radiographs remain necessary for monitoring various other parameters, including the amount of lengthening and axial bending. There is interest in the use of these compulsory images for quantitative callus assessment and to avoid the additional effort and cost relating to DEXA.

Based on our investigation, BMD ratio and pixel value ratio are reasonably well correlated. However, a separate study in animals, comparing pixel value ratio with mechanical strength of the callus, may be required to prove this concept. There is little information regarding the use of pixel value for measuring callus mineralization. Shim et al found that serial pixel values within the callus followed a sigmoid curve. This is explained by the fact that during bone healing mineralization only starts with some delay [15].

The disadvantage of this technique is that pixel value is affected by the presence of metal in the vicinity of the point of measurement, as the presence of metals leads to an abnormally low pixel value of that area, suggesting increased radiopacity of that area. Thus, if there is any metal nearby, repeat imaging has to be done or evaluation has to be by some other method, but most of the methods used for estimation of bone mineralization are affected by the presence of metal in nearby fields. Young et al. studied this problem in patients with Ilizarov fixators and recommended that X-ray beams be parallel to the Ilizarov ring that is nearest to the distraction site to minimize the chance of the presence of metal at the site of interest [19]. The other disadvantage of this study was that we took the proximal segment as a control to obtain the ratio, which was relatively smaller than the distal segment in all cases, so we could not take as many reading as we did in the regeneration area. The part distal to the osteotomy usually undergoes osteoporosis during the period of fixation. Up to 40% loss of original bone mineral content has been reported [6]. That was the rationale of our taking the proximal segment as the control, in spite of doing a DEXA scan of the entire tibia.

To conclude, pixel values measured on standard radiographs appear to indicate callus stiffness and may obviate the use of DEXA.

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