Digital image analysis of bone allograft union in sheep

Franck Bresler[1], Patrick Simon[2], Daniel Schmitt[1], Michel Verhelpen[4], Michèle De Gasperi[3] and Christian Delloye[4]

We compared the reliability of computer-assisted radiographic analysis (CARA) and visual evaluation of radiographs to assess host-graft junctions. 68 host bone/allograft junctions were obtained from an ongoing study on bone allografting in sheep. At 6 months, the grafted tibias were explanted and healing of the host-graft junctions were macroscopically determined. 49 junctions were macroscopically healed, whereas 19 had not united. 51 (0.8) of the junctions were correctly classified by radiographs, while 63 (0.9) of the junctions were correctly classified by CARA (p = 0.03). These findings warrant further evaluation in a clinical setting.

[1]Clinique de Traumatologie et d'Orthopédie, Rue Hermite, 49, FR-54000 Nancy, France. Tel +33 3838575-25. Fax -51; [2]Service de chirurgie orthopédique Pr Babin, Hôpital Hautepierre, CHU, Avenue Molière, 67098 CEDEX, FR-Strasbourg, France, [3]Service d'Informatique Médicale, Faculté de Médecine, Université de Nancy I, 9 avenue de la Forêt de Haye, 54500 Vandoeuvre les Nancy, France, [4]Orthopaedic Research Laboratory, Faculté de Médecine, Université Catholique de Louvain, 53, avenue Mounier, BE-1200 Bruxelles, Belgique.
Submitted 97-02-25. Accepted 97-11-03

Evaluation of bony union on radiographs is subjective and depends on, among other things, orientation of the beam and film exposure. Moreover, with bone allografts, the callus often becomes visible later and the osteotomy line, in many cases, persists more than 1 year. Computer-assisted densitometric image analysis may be better for radiographic assessment of various bone conditions and has been successfully applied in periodontology (Bragger et al. 1991, Dubrez et al. 1992). Digital analysis of radiographs can be used to quantify bone density changes which occur across an osteotomy line during bone healing.

From an ongoing study of massive bone allografts in sheep we compared data from computer-assisted analysis of digitized radiographs with visual evaluation of radiographs and mechanical assessment of host bone/ allograft junctions.

Material and methods

Experimental model

A 5-cm osteoperiosteal segmental defect was made in the tibial mid-diaphysis of the left limb of adult sheep. A tibial allograft was then implanted to fill the defect and was fixed with a custom-made locked tibial nail. The animals could bear weight 1 day after surgery and were observed for 6 months. At that time, they were killed with an overdose of phenobarbital. The whole tibia was explanted and the hardware removed. The proximal and distal junctions were macroscopically examined for union and then radiographed.

68 junctions between host bone and allografts from 34 animals were studied.

Macroscopic mechanical assessment

At the time of harvesting, each junction was manually evaluated in flexion and shear and was classified as healed = no apparent mobility; nonunion = any residual mobility. This assessment served as the reference for the healing process in the study.

Radiographic analysis

Standardized radiographs with anteroposterior and lateral views of each allografted bone were obtained, using Kodak X-Omat high definition film, 24 × 30 cm. Each junction was separately evaluated by 3 examiners (a bone radiologist and two senior orthopedic surgeons). This evaluation was repeated twice at a monthly interval. Each radiograph was classified into 3 categories: healed, uncertain healing, nonunion.

Computer-assisted radiographic analysis (CARA)

Radiographs were digitized with a high-resolution commercial black and white CCD camera (Sony SSC-M370CE, 752 × 582 pixels, Sony Corp., Japan)

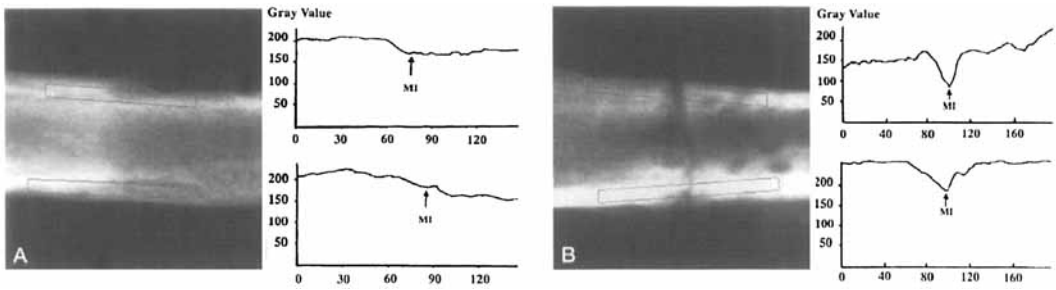

Figure 1. CARA evaluation of a macroscopically healed (A) and a macroscopically unhealed (B) junction. Radiographic aspect of the junction with defined cortical regions of interest and their corresponding CARA histograms (grey-level correlated with the pixel data). MI represents the minimal grey-level of the junction interfaces.

and a frame-grabber hardware card (Data Translation, DT3851-4, Marlboro, MA, USA), using a microcomputer (PC-IBM-486DX50). The image-processing software (Global Lab Image 3.0, Data Translation, Marlboro, MA, USA) allowed capture of a frame on board with a resolution of 752 × 512 × 8 bit pixels. To correct for density alterations, the grey-level histograms of each image background and host-bone cortices were compared and adjusted. We measured the optical density of regions of interest of 15 pixels of the full thickness cortical bone on either side of the osteotomy line. A histogram of density values was obtained. The mean grey-value of the cortical host bone (MH) and the minimal grey-value (MI) of the osteotomy line could thus be calculated for each cortical bone junction (Figure 1). The density ratio (DR) of the host-graft interface, as expressed by the MH/ MI ratio, was used to evaluate the quality of host-graft union. As there were 2 osteotomy lines to be analyzed for each graft in the anteroposterior and lateral views, four ratios were available for each graft and an average value was derived.

Statistics

Interobserver reliability of radiographic assessment was evaluated using Kappa reliability coefficients. Since the variance between the healed and unhealed groups was not similar in the CARA assessment, a non-parametric test (Mann-Whitney) was used. The sensitivity (proportion of macroscopically unhealed junctions also assessed such junctions with CARA) and the specificity (proportion of macroscopically healed junctions also assessed such junctions with CARA) were determined for each density ratio computed from CARA. They were represented on a receiving operating characteristic curve (ROC) (Altman 1991). The ROC curve was used to determine the cutoff value of the density ratio corresponding to the highest accuracy (minimal false negative and false positive results). Comparison of the percentage of correctly classified junctions was performed using the chi-square test. All differences were considered significant at a probability level of 95% ($p < 0.05$).

Results

At 6 months, 49/68 junctions had healed macroscopically.

In the radiographic evaluation, kappa values between observers 1 and 2, 2 and 3, 1 and 3 were, respectively, 0.97, 0.96, and 0.97. As the degree of agreement was excellent, we used the results of observer 1, who found that 35 junctions were radiographically healed and 17 were not united. In 16 junctions, the degree of radiographic union could not be determined. Radiographic and macroscopic evaluations were in agreement for the union and nonunion groups, except in 1 macroscopically healed junction that was evaluated as not united on radiographs. In the radiographically unclassified group, 3 were healed macroscopically and 13 were not. Thus, 52/68 (0.8) of the junctions were correctly classified on radiographs.

Using CARA, a highly significant difference in the mean density ratio (DR) was observed between the macroscopically healed and unhealed junctions, being 1.2 (SD 0.03) and 2.5 (SD 0.4) ($p = 0.0001$), respectively (Figure 2). The CARA criteria for union were determined, using a ROC curve. A junction was considered healed when its density ratio was lower than 1.56 (sensitivity rate 79%, specificity rate 98%). Using this value, 52 junctions were considered healed and 16 not. 48/49 macroscopically healed junctions and 15/19 macroscopically unhealed junctions were correctly classified by CARA. Thus, 63/68 (0.9) of the junctions were correctly classified by CARA. This ratio was better than the one obtained with radiographs ($p = 0.03$). Among the 5 false CARA results, two situations were identified: overestimation of healing when an exuberant callus enveloped the cor-

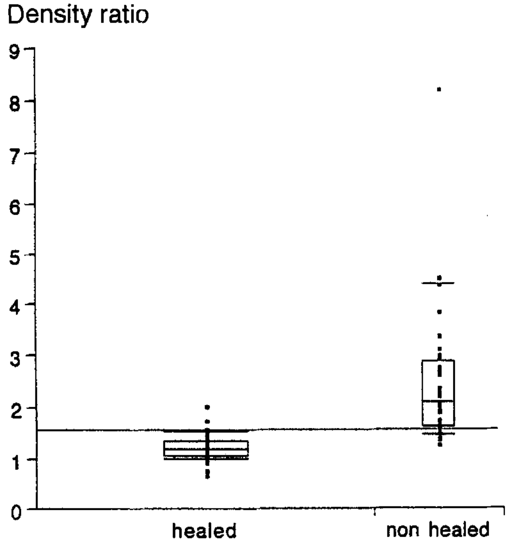

Figure 2. Distribution of CARA density ratio values of macroscopically healed and unhealed junctions.

tex without real union (4 cases); conversely, underestimation of union occurred when a large uniting callus developed and the osteotomy line persisted (1 case).

Discussion

In a study of massive retrieved human allografts, Enneking and Mindell (1991) showed a good correlation between radiographic evidence of union and macroscopic observations, but they also noted some errors that underline the lack of accuracy and objectivity in the visual radiographic evaluation. We found CARA, which is technically accessible, not invasive, and not hardware-dependent (even in cases with plated junctions when the measurement of optical density would be possible) more reliable for assessing bone healing. This technique still has some limitations. In our evaluation, only the cortical bone density variation was addressed, in order to exclude the potential influence of a surgical implant. The external callus and medullary area were not included in the region of interest which might cause both over- and underestimates of healing. Taking the external callus into account in clinical practice might further increase the reliability of CARA.

Acknowledgements

The authors gratefully acknowledge help from Mrs C. Hancotte, A. Schmitz, P. Delhaye for skillful preparation of this study and from Professor Alain Blum for his valuable advice with statistical analysis. The study has been partly funded by the Belgian Fonds National de la Recherche Scientifique (FNRS).

References

Altman D G. Practical statistics for medical research. Chapman & Hall, London 1991.

Bragger U, Burgin W, Lang NP, Buser D. Digital subtraction radiography for the assessment of changes in peri-implant bone density. Int J Oral Maxillofac Implants 1991;6: 160-6.

Dubrez B, Jacot-Descombes A, Pun T, Cimasoni G. Comparison of photodensitometric high-resolution digital analysis of bone density from serial dental radiographs. Dentomaxillofac Radiol 1992; 21: 40-4.

Enneking W F, Mindell E R. Observations on massive retrieved human allografts. J Bone Joint Surg (Am) 1991; 73: 1123-42.