Letters to the Editor

Concerns About the Effects of Platelet Concentrate

To the Editor:

We read with interest the article by Orrego et al.[1] entitled "Effects of Platelet Concentrate and a Bone Plug on the Healing of Hamstring Tendons in a Bone Tunnel." We congratulate the authors on their very interesting work; however, we have several concerns regarding their methods and conclusions.

The clinical outcome of anterior cruciate ligament reconstruction by use of a hamstring tendon graft depends on the biologic integration between the tendon and the bone. The healing process starts immediately after the operation. The empty space between the tendon and the bone is replaced with an increasing number of fibroblasts in a few days. At 3 weeks, small vessels are evident, along with an increased number of osteoblasts on the bone surface. After 6 weeks, the vessels decrease in number, along with a shield-like new bone formation surrounding the tendon and an increased number of collagen fibers integrated along the tendon. At 12 weeks, the tendon is practically directly attached to the bone.[2]

Because of technical difficulties, knowledge about the ligament graft-healing process in humans is limited, but available data have shown that a complete integration of the graft with the surrounding bone occurs as early as 12 weeks.[3] Platelet-derived growth factors (PDGFs) regulate the graft-healing process. They stimulate angiogenesis, cell proliferation, and collagen synthesis. Increased levels of PDGFs were observed within the healing area in the early postoperative period, reaching the greatest expression at 3 weeks after implantation. Thereafter the concentration of PDGFs decreased and returned to the preoperative level at 12 weeks postoperatively.[4]

On the basis of the mentioned scientific data, we suggest that new studies should consider several facts. First, the current study design with the follow-up postoperative evaluations at 3 and 6 months is inappropriate. As we know, the graft integration into the tibial and femoral tunnel is usually complete by 12 weeks. After that period, the pullout test showed the graft's rupture intra-articularly only.[5,6] Therefore the role of PDGFs in postoperative graft healing in the bone tunnel should be monitored within the first 3 months.

Second, Orrego et al.[1] assessed the graft integration according to the presence of an interface between the graft and bone tunnel walls with magnetic resonance imaging scans. The absence of an interface should reflect the major integration and maturation of the graft. We think that graft integration is a complex and gradual process, which cannot be assessed after only 2 phases. It is not a cascading process but rather an integrating process. Therefore graft healing in the bone tunnel should be assessed with a more sensitive method, such as the quantitative evaluation of angiogenesis by use of magnetic resonance angiography.[7]

Finally, Orrego et al.[1] clinically evaluated all patients using the Lysholm and International Knee Documentation Committee scores preoperatively and again at 6 months after surgery. It is our opinion that we cannot expect any major differences between the trial groups based on their functional scores as late as 6 months after surgery, because the rehabilitation period is practically complete by then, even in the cases without PDGF treatment. In our opinion the main rationale of using PDGFs is to accelerate healing and to finish the rehabilitation process earlier (i.e., in 4 to 5 months). We also think that it would be much more interesting to evaluate postoperative anteroposterior knee stability by comparing the PDGF group and control group by using the KT-2000 arthrometer.

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Author's Reply

We thank Drs. Vogrin, Rozman, and Haspl for their letter referring to our article published in the December 2008 issue of *Arthroscopy*. Clearly, their analysis reflects an important interest regarding the topic. Nevertheless, we believe that some of the statements on which their critique is based have to be carefully examined. Specifically, it would be somewhat risky to affirm that "a complete integration of the graft with the surrounding bone occurs as early as 12 weeks." Although it is true that a lot of information can be found when doing a thorough search of the literature for different animal models, including the studies of Kohno et al.[1] in rabbits and Kuroda et al.[2] in dogs, as Vogrin et al. referenced in their letter, mentioning periods of fewer than 3 months, it does not seem reasonable to extrapolate the results obtained too categorically. The literature review carried out by Ekdahl et al.,[3] mentioned by Vogrin et al., only mentions 2 articles, both of which are case reports of humans with reference to integration periods of fewer than 3 months. It is worth emphasizing that in our study, magnetic resonance imaging changes between the third and sixth month existed and that at 6 months, there was a variable percentage of immature grafts according to the observed parameters. Therefore it seems reasonable to think that the graft healing process takes more time in humans than in animals.

We agree with the statement of Vogrin et al. that the absence of an interface should be a sign of major graft integration, and we considered it so in our study. Regarding the evaluation of angiogenesis with magnetic resonance angiography, the study mentioned by Vogrin et al. reported progression of revascularization of between 9 and 22 months, showing important changes in this period.[4] This confirms that there are subsequent variations with long periods of time whose interpretation makes it even more complex to affirm the sensibility of using this method as an instrument to measure early graft healing.

Understanding the spirit of the critique of Vogrin et al., we sincerely hope that on the basis of the open discussion hereby established, new studies can be designed that may clarify the numerous unresolved questions that still exist regarding this topic.

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