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CORR Insights®: Is the Induced-membrane Technique Successful for Limb Reconstruction After Resecting Large Bone Tumors in Children?

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Where Are We Now?

The treatment of children with malignant bone tumors has improved dramatically during the last 40 years. With improve-

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ments in multiagent chemotherapy, and advances in surgical techniques, limb salvage has become the standard treatment option. Several reconstruction approaches are employed to provide a functional and durable extremity. Although initial studies confirm that limb-salvage surgery carries no greater risk of local recurrence or mortality compared with amputation [6], complications are common, and concerns about late revisions in this patient population remain [4]. Skeletal reconstruction with prosthetic components, large-allograft bone segments, autograft techniques, free fibula transfers, and novel autograft procedures (such as the “turn-downplasty” knee arthrodesis [9]) all have had some success. However, durable and functional reconstructions can be difficult to obtain, particularly in children. A biological answer for

skeletal reconstruction would be to replace the missing segment with living bone, which could remodel and strengthen in time. This is thought to be an attractive approach.

Surgeons have attempted biologic reconstructions of diaphyseal bone resections using allografts, free vascularized fibular transfers, and combinations of both. Traditionally, such intercalary reconstructions are considered among the better allograft reconstruction options. However, a recent review by Bus and colleagues [2] found an overall complication rate of 76% with this type of reconstruction, particularly when the graft segments exceeded 15 cm in length. Similarly, a recent study by Schuh and colleagues [7] found a 65% revision/reoperation rate for autologous fibula reconstructions (both vascularized and non-vascularized) and a 25% nonunion rate. In addition to such complications, the long-term goal of a viable skeletal reconstruction using allografts has been elusive. In their classic paper, Enneking and Mindell [3] clearly demonstrated

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incomplete healing and remodeling of large allografts with larger portions of the allografts remaining nonviable even years after their implantation.

Where Do We Need To Go?

The current study by Fitoussi and colleagues presents an interesting case series of pediatric patients who were treated with intercalary skeletal reconstructions using the “induced membrane technique” after malignant bone tumor resections. In their study, the authors described treating eight adolescent patients for malignant primary bone tumors (osteosarcoma and Ewing sarcoma) in three anatomical locations (proximal humerus, femur, and tibia) during a 10-year period. All of the patients were adolescents (ages 11 to 17) and had diaphyseal skeletal defects of more than 15 cm following the tumor removal. In contrast to the usual technique described for induced membrane grafting, autograft placement—or the second-stage of the reconstruction—was delayed in order to allow administration of adjuvant chemotherapy to the patients. By placing a stable antibiotic spacer and creating a hospitable environment for future grafting, the intent was to create a durable biologic reconstruction of the bony defects. The authors also modified the technique by adding an autologous fibula to the

cancellous bone graft. They did this to improve initial stability of the reconstructions. The skeletal integrity of these reconstructions still needs to be demonstrated in a long-term followup study. How durable will these weight bearing, long bone reconstructions be over time?

Although the induced membrane method has been well-studied and reported on in the last 12 years [1, 8], the technique has usually been described in adults and primarily employed for posttraumatic defects. Pelissier et al. [5] reported that the best timing for the active membrane effectiveness, with highest cytokine concentrations, is 4 weeks to 6 weeks after placement of the antibiotic-cement implant. Because this timeframe is not possible for the children receiving adjuvant chemotherapy, the patients in the current study had the second stage of the grafting procedures months after the initial resection operation. The biology behind the technique is interesting and the questions that are raised here, particularly by the addition of chemotherapy and delayed second stage grafting provide several areas for further study.

How Do We Get There?

The induced membrane method of skeletal reconstruction for tumor diaphyseal appears to hold promise, but important long-term information

on the patients and their reconstructions is lacking. Although the current study covers longer than a 10-year interval; six of the eight patients have 3 or less years of followup. From an oncological standpoint, additional work must be done to confirm that there is no increased risk for local tumor recurrence, particularly when employing biologic techniques, which depend on growth factors and cytokines to promote bone formation in order to reconstitute a skeletal defect.

Additionally, further basic research will be needed to evaluate the biology of the membrane, the effect of delayed grafting, the possible effects of chemotherapy, and potential means to improve or speed up the processes. Clinical studies with larger numbers of patients and longer clinical followup will be needed to confirm the intriguing early results of the paper. One area researchers should focus on is the long-term durability and stability of these grafts. For example, the longer reconstructions, and particularly those associated with adjacent joint arthrodesis such as the humeral reconstructions reported in the current study, may be prone to repeated mechanical stress and fatigue failures. As reported in the current study, during the limited followup period, three grafted segments out of eight fractured, all within the first 2 years. Long-term studies should focus on whether additional fractures will

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occur in the cohort of healed patients or will the bone regenerate and sufficiently hypertrophy to prevent future fractures. Such a clinical evaluation may require “a multiinstitutional cooperative study” in order to evaluate sufficient numbers of reconstructions. Lastly, the technique described requires tumor resection, placement of the spacer and after months of chemotherapy, delayed grafting, with the possible addition of other procedures in the future as well as relatively long periods of limited activity. From the patient perspective, the effect of this prolonged treatment on the emotional and overall medical wellbeing of the patient should be evaluated.

Additional investigation and close patient followup may answer some of our questions about this innovative technique, as well as provide appropriately selected patients with a viable long-term answer, or “biological” reconstruction, which up to this point in time has been an elusive goal.

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