

## SPECIALTY UPDATE

## What's New in Orthopaedic Oncology

Santiago A. Lozano Calderón, MD, PhD, Kevin A. Raskin, MD, Francis Hornicek, MD, PhD, and Joseph H. Schwab, MD, MS

*Investigation performed at the Orthopaedic Oncology Service, Department of Orthopaedic Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts*

### Malignant Primary Bone Tumors

#### Ewing Sarcoma

Ewing sarcoma is associated with balanced translocations of the EWS and ETS genes that produce a fusion protein that binds DNA affecting transcription. Two new studies identified targets of the EWS/FLI1 fusion protein. One study showed preferential binding for a DNA region that induced early growth response 2 (EGR2) expression. EGR2 stimulates proliferation, differentiation, and survival of neural crest-derived cells, from which Ewing sarcoma cells are thought to originate. An EGR2 gene knockdown halted Ewing sarcoma cell growth in vitro and in a xenograft model, demonstrating that the EWS/FLI1 fusion protein works through EGR2<sup>1</sup>. A second study showed that EWS/FLI1 targets SLFN11, which is highly expressed in some Ewing sarcomas. Ewing tumors expressing SLFN11 were susceptible to topoisomerase inhibitor treatment<sup>2</sup>. In a separate genetic study, 116 patient samples of Ewing sarcoma were used to identify somatic mutations. The gene for fibroblast growth factor receptor 1, FGFR1, was noted to have a gain in copy number in 31.7% of primary tumors. Furthermore, RNA interference of FGFR1 expression halted the growth of Ewing sarcoma cells in a xenograft model. The study concluded with a patient example in which treatment with a tyrosine-kinase inhibitor against FGFR1 reduced 18-FDG-PET (<sup>18</sup>F-deoxyglucose positron emission tomography) activity<sup>3</sup>.

Margulies et al. developed an animal model for Ewing sarcoma treated with radiation therapy. Increased osteoclastic activity without detection of RANKL (receptor activator of nuclear factor  $\kappa$  ligand) in bone affected by the

tumor was identified. MCSF (macrophage colony stimulating factor) rather than RANK ligand mediated osteoclastic activity<sup>4</sup>.

Two studies evaluated medical treatment. The Children's Oncology Group compared the effectiveness of a surgical procedure with that of radiation in a group of 465 patients managed with standardized chemotherapy. Surgical procedures were associated with lower local failure rates, but this did not translate into significant differences in event-free survival, overall survival, or distant metastasis<sup>5</sup>.

The Brazilian Collaborative Study Group published its results of risk-adapted intensive therapy with carboplatin in a developing country. At five years, event-free survival was 51.4% and overall survival was 54.4%. At five years, event-free survival was 67.9% for patients with localized disease and 25.5% for patients with metastatic disease. The five-year overall survival was superior in patients with localized disease at 70.3% compared with patients with metastatic disease at 29.1%. Multivariate analysis demonstrated metastatic disease to be the only significant prognostic factor. The authors concluded that clinical outcome was comparable between industrialized and developed countries<sup>6</sup>.

The level of sport activity in thirty long-term survivors of Ewing sarcoma after limb salvage was assessed at a mean follow-up of sixteen years. Surgical procedures included resection without reconstruction (eight patients), biologic reconstruction (nine patients), and endoprosthetic reconstruction (thirteen patients). Eighty-three percent of patients were performing athletic activity regularly. Patients with pelvic and femoral resections with no reconstruction exercised more hours per week than those with endoprosthetic pelvic reconstruction. Biologic reconstructions did not limit high-impact sports. The authors concluded that long-term survivors can

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achieve high levels of sport activity after the surgical procedure for limb salvage<sup>7</sup>.

The same group evaluated long-term survivors of Ewing sarcoma for low bone mineral density and increased pathologic fracture risk. Fifty-six patients were evaluated with questionnaires and bone mineral density. Thirty-one patients (55%) had abnormal bone mineral density, seven patients (13%) had osteoporosis, and twenty-four patients (43%) had osteopenia. Association between low bone mineral density and fracture events was not seen<sup>8</sup>.

### *Osteosarcoma*

Multiple studies improved our understanding of pathophysiology in osteosarcoma. Many of these are opening doors for new therapeutic options. The CDK11 gene is essential for osteosarcoma cell growth and survival. Feng et al. proved that CDK11 can be silenced efficiently by CRISPR (clustered regularly interspaced short palindromic repeats)-Cas9, decreasing cell proliferation and viability and inducing apoptosis in osteosarcoma cell lines (KHOS, U-2OS)<sup>9</sup>. Glut-1 (glucose transporter protein-1) expression was found to be a potential predictor of survival in patients with osteosarcoma. Additionally, glucose metabolism was found to be negatively associated with angiogenesis<sup>10</sup>.

Lastly, sixteen patients with phase-I or II osteosarcoma expressing HER2 (human epidermal growth factor receptor 2) were treated with HER2-chimeric antigen T-cell infusions. The chimeric antigen receptor (CAR) technology takes advantage of antigens expressed on the tumor and not on normal cells. The patient's lymphocytes are extracted and modified to target tumor cells; then they are reinjected into the patient. CAR therapy does not require tumor cells expressing HLA (human leukocyte antigen)-class-1 antigens for lymphocytes to recognize target antigens. HER2-CAR T cells still could be identified at six weeks and their concentration was dependent on the initial infusion dose. The authors concluded that combining HER2-CAR therapy with other immunomodulating agents provided a foundation for forthcoming agents in osteosarcoma<sup>11</sup>.

Margin status is crucial when treating high-grade osteosarcoma. A retrospective study from the Moffitt Cancer Center on fifty-one patients who underwent a surgical procedure with curative intent and chemotherapy, following National Comprehensive Cancer Network (NCCN) guidelines, found that positive margins were associated with higher rates of local recurrence. Overall survival was also worse in patients with local recurrence. The authors reported five positive margins (10%) and a local recurrence rate of 14% (seven margins)<sup>12</sup>. Another study focused on osteosarcoma cases in which the knee joint was spared by leaving the distal femoral epiphysis and then reconstructing the defect with intercalary allograft. The overall survival rate was 86%, with three local recurrences (9%) in the soft tissues but none in the remaining epiphysis<sup>13</sup>.

Takeuchi et al. analyzed factors affecting survival and relapse after treatment of forty-five locally recurrent osteosar-

comas. The long-term prognosis was poor (13% survival at ten years). Independent risk factors included a recurrent tumor that was  $\geq 5$  cm and metastatic disease at presentation. Most recurrences were in soft tissues and were difficult to see in radiographs. Early detection is necessary given the impact of tumor size on survival. Resection with wide negative margins is critical to optimize outcome<sup>14</sup>.

Function in osteosarcoma survivors in the long term after endoprosthetic reconstruction of the knee is not fully understood. Lang et al. reported on twenty-seven patients seen at one, three, and five years and the latest follow-up. Reduction in high-impact activities was observed. Further functional improvement was not evident after five years, and patients with a higher level of sport activity before the surgical procedure had a higher level of activity at the time of follow-up<sup>15</sup>.

### *Chondrosarcoma*

Otero et al. used a rat model to demonstrate the role of osteoclastic activity in chondrosarcoma. In their model, rats treated with zoledronic acid had less sarcoma-mediated bone destruction and tumor growth<sup>16</sup>. Sun et al., using microRNA (miR) expression, analyzed two primary bone chondrosarcomas and normal articular cartilage for the effects of hypoxia and HIF-1 $\alpha$  (hypoxia inducible factor-1 $\alpha$ ). The authors found overexpression of miR-181 in both chondrosarcomas and the JJ cell line when compared with cartilage. This enhances VEGF (vascular endothelial growth factor) expression that can be inhibited by anti-miR-181a, opening new potential therapeutic options<sup>17</sup>.

### *Chordoma*

PD-1 (programmed death-1) and its ligand PD-L1 have been the subject of many cancer studies because of the early success of recently available agents targeting their interaction. One study found fewer than 5% of chordoma cell lines expressing PD-L1. However, the expression of PD-L1 was inducible with the addition of interferon- $\gamma$ . The authors also explored the expression of PD-L1 in tumor samples but found no expression in ten tested tumors. Tumor-infiltrating lymphocytes expressed PD-1 in three of the six tested samples<sup>18</sup>. In contrast, Feng et al. found that 95% of seventy-eight patient chordoma samples expressed PD-L1 in a tissue microarray. The expression of PD-L1 correlated with tumor-infiltrating lymphocytes, which were prominently found in 30% of cases<sup>19</sup>.

Froehlich et al. investigated the expression of survivin in fifty chordoma samples and three chordoma cell lines. Transient knockdown of survivin (by YM155) led to G2/M arrest, decreased proliferation, and increased polyploidy and apoptosis<sup>20</sup>. Osaka et al. found miR-155 expression to be high in biologically active chordoma. This expression was validated by RT-PCR (reverse transcription polymerase chain reaction). miR-155 independently affected chordoma prognosis<sup>21</sup>.

A pilot study tested FMISO-PET/CT (<sup>18</sup>F-fluoromisonidazole positron emission tomography/computed tomography) for

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visualization of tumor hypoxia in patients with chordoma of the mobile and the sacrococcygeal spine. Imaging in twenty patients before radiation and after 19.8 to 34.2 Gy of relative biologic effectiveness detected tumor hypoxia feasibly. Further studies using double-baseline FMISO-PET/CT and hypoxia-directed radiotherapy dose escalation are future lines of research<sup>22</sup>.

Xie et al. reported on the long-term outcome of thirty patients with recurrent sacral chordoma treated surgically. At a mean follow-up time of 3.8 years, the authors found survival of 89% at two years, 56% at five years, and 19% at ten years. Incomplete resection resulted in survival of 54% at two years and 36% at five years. Wide resection gave the best chance of long-term survival and complete resection of local recurrence gave the best chance of disease control<sup>23</sup>.

### Malignant Soft-Tissue Sarcomas

On the basis of clinical data and two distinct animal models, YB-1 was proved to be a critical regulator of HIF-1 $\alpha$  expression in sarcoma cells. This is important because of the implications in metastasis mechanisms in patients with sarcoma<sup>24</sup>.

Obesity is a known predictor of complications after surgical procedures. Adipose tissue is also known to promote a favorable microenvironment for tumor growth. The correlation between obesity and survival, local recurrence, and wound complications in patients with extremity soft-tissue sarcoma treated surgically was evaluated by comparing 154 obese patients (those with a body mass index [BMI] of  $\geq 30$  kg/m<sup>2</sup>) with 243 non-obese patients (those with a BMI of  $< 30$  kg/m<sup>2</sup>). Regression analysis confirmed that obesity did not affect survival, local recurrence, or wound infection<sup>25</sup>.

Prognostic biomarkers are scarce in soft-tissue sarcoma. Panotopoulos et al. reported on eighty-five patients with liposarcomas in whom association between elevated alkaline phosphatase and CRP (C-reactive protein) and reduced disease-specific survival was seen<sup>26</sup>. Pretell-Mazzini et al. reviewed current concepts in the management and prognosis of unplanned soft-tissue sarcoma excisions, emphasizing prevention and appropriate referral<sup>27</sup>.

### Benign Bone Tumors

#### Tenosynovial Giant Cell Tumor

The management of tenosynovial giant cell tumor is evolving as new agents targeting receptors known to be important in its pathophysiology are introduced. CSF1 (colony-stimulating factor 1) is produced by neoplastic cells in the tenosynovial giant cell tumor. Many of these have a translocation linking CSF1 on chromosome 1 to COL6A3 on chromosome 2. The interaction of CSF1 with its receptor CSF1R can be targeted with PLX3397, a synthetic compound that binds to CSF1R, preventing its activation by CSF1. A recent phase-1 trial enrolled forty-one patients in its dose-escalation arm, followed by another twenty-three patients in the study extension arm. Of the twenty-three patients in the extension arm, twelve had

partial responses to treatment and seven had stable disease after a median therapy time of eight months. This is a useful example of targeting oncogene-driven neoplasms for therapeutic purposes<sup>28</sup>.

#### Giant Cell Tumor of Bone

Giant cell tumor of bone was the subject of a retrospective study investigating pulmonary metastasis risk factors in 167 patients followed for at least two years. Eleven patients (6.6%) had biopsy-proven pulmonary metastasis. Tumors of the axial skeleton, stage-3 disease, and local recurrence were associated with higher metastatic rates. Younger patients had higher metastatic rates and may benefit from closer follow-up according to the authors. Multivariate analysis identified local recurrence as the strongest independent predictor of pulmonary metastasis. Ten of the eleven patients with metastatic disease were treated with resection of the metastatic lesion, with none of the eleven patients dying from giant cell tumor<sup>29</sup>.

#### Cartilage Tumors

A large multicenter, retrospective study focused on clinical presentation and outcomes in 199 operatively treated patients with chondroblastoma of the extremities. Most patients were treated with curettage and packing with autograft or allograft bone (94.4%). One hundred and twenty-six patients had at least a twenty-four-month follow-up. The local recurrence rate was 4.8%. The proximal part of the humerus was noted to have the highest local recurrence. The authors suggested that local recurrence may be more common in patients with open physes<sup>30</sup>.

Two articles addressing malignant transformation in the setting of multiple hereditary exostosis were published recently. In one study, malignant transformation rates were assessed in patients with multiple hereditary exostosis using online survey software addressed to patients using online social networks and support group web sites. Seven hundred and fifty-seven patients from forty-one countries responded to the survey. Patients had a mean of seven multiple hereditary exostosis-related operations in their lifetime. Twenty-one patients (2.8%) reported having developed a chondrosarcoma; of these chondrosarcomas, eight occurred in the pelvis and four occurred in the scapula. The mean patient age at the time of the initial diagnosis was 5.4 years and the mean patient age at the time of malignant transformation was 28.6 years. The authors reported a possible bias toward patients with advanced disease, as these may be more likely to use support groups<sup>31</sup>.

The presence of intraosseous chondroid lesions in patients with multiple hereditary exostosis was investigated using a prospectively collected nationwide Dutch database. The study found that seven (3.6%) of 195 patients had intraosseous chondroid lesions. Five of these patients developed chondrosarcomas. All seven patients had either exostosin-1 or exostosin-2 mutations. The authors concluded that identification of a seemingly innocuous chondroid lesion in multiple hereditary

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exostosis should prompt vigilant follow-up for malignant transformation<sup>32</sup>.

### ***Aneurysmal Bone Cyst***

Wang et al. reported on high-speed burring treatment without other adjuvants in thirty-one patients with an aneurysmal bone cyst (only one recurrence, 3.2%). Curettage, high-speed burring, and bone-grafting proved to have equivalent recurrence rates when compared with other techniques in which adjuvants are used<sup>33</sup>.

### **Bone Metastasis**

Lysyl-oxidase, produced from the LOX gene, has previously been associated with metastatic potential in estrogen receptor-negative breast cancer [ER(-)BCa]. LOX is activated and is secreted under hypoxic conditions. Researchers have now shown that LOX activity in ER(-)BCa is associated with bone metastasis over other visceral sites of distant spread. Additionally, LOX-directed bone resorption preceded metastatic cells' arrival, providing a bone environment where these could grow. LOX activated osteoclasts independently from RANKL. This has implications for our understanding of bone physiology and metastatic disease<sup>34</sup>.

Predicting survival in patients with bone metastasis often helps in directing care. A previous published model using Bayesian methodology was validated in an Italian population. This model relies on ten prognostic factors. The Bayesian model was able to predict survival with areas under the curve of 0.80 at three months and 0.77 at twelve months<sup>35</sup>. A separate study compared three methods of predicting survival including a classic scoring system, nomograms, and a boosting algorithm using 927 patients. The authors identified low BMI (<18.5 kg/m<sup>2</sup>) and the presence of other comorbidities as new predictors. The boosting algorithm outperformed the other methods on the training sets, but the nomogram matched the boosting method on the test set. Furthermore, the nomogram is simpler to apply without the need for advanced statistical software<sup>36</sup>.

Femoral cephalomedullary implants are often chosen to protect the femoral neck from potential future metastatic disease in patients with diaphyseal lesions. Moon et al. reviewed 145 rods inserted to treat diaphyseal lesions. Postoperative images did not demonstrate any new lesion in the femoral neck over time. Their findings question the routine use of cephalomedullary devices in this patient population<sup>37</sup>.

Renal-cell and thyroid carcinoma are highly vascular tumors in which preoperative embolization is often advocated to mitigate bleeding. A matched case-control study with forty-one cases in each arm assessed the value of preoperative embolization in open intramedullary nailing and in closed intramedullary nailing. In cases in which the tumor was opened for curettage, preoperative embolization was associated with lower bleeding volume, shorter operative time, and fewer blood transfusions. In closed procedures, there was no differ-

ence in transfusion volume. The authors recommended embolization for open procedures only<sup>38</sup>.

CT is becoming a common tool to assess bone rigidity in situations of potential pathologic fracture. New applications of this technique were published recently. Damron et al. reported the multi-institutional experience with 125 patients who prospectively underwent CT scanning of both femora using phantoms of known density (CT-based structural rigidity analysis [CTRA]). Enrolling physicians were allowed to decide between operative and nonoperative treatment. Risk of fracture according to CT was defined as a reduction of  $\geq 35\%$  in axial, torsional, and bending rigidity. A high-risk fracture was defined as one with a Mirels score of  $\geq 9$ . CTRA had higher sensitivity, specificity, and predictive values in detecting impending pathologic fractures than the Mirels classification<sup>39</sup>. The same group tested the influence of CTRA on decision-making in simulations of bone metastasis and found little effect<sup>40</sup>. However, in an additional investigation, they found that availability of CTRA significantly influenced the treatment plan and the prediction of fracture events by the surgeon<sup>41</sup>.

Perioperative blood transfusions are known to increase cancer recurrence and to decrease patient survival in patients with primary malignancies. Janssen et al. evaluated the impact of blood transfusion in patients with metastatic disease of long bones after surgery. In a retrospective review of 789 patients, perioperative allogenic blood transfusions did not decrease survival in this population. However, a dose-response effect with lower survival in patients receiving more transfusions was identified<sup>42</sup>.

Metastatic melanoma in bone is a poor prognostic factor, with palliative treatment being the treatment of choice. Krygier et al. reported on thirty-seven patients who underwent forty-one procedures. Twenty patients had pathologic fractures. A higher recurrence rate in patients with failed radiation therapy who did not have wide excision of osseous metastases was observed. The importance of local control of bone disease and resection of osseous metastasis in patients with failed prior radiation was highlighted<sup>43</sup>.

### **Reconstruction**

#### ***Spine***

Luzzati et al. presented their experience with multilevel en bloc spondylectomy in neoplastic disease. The outcome was satisfactory in thirty-four patients. The complication rate was 65%, with most patients recovering from the complications. The surgical procedure is challenging, but satisfactory intermediate-term results can be obtained<sup>44</sup>.

Moran et al. reported the functional outcome of sacrectomies after reviewing seventy-three patients. The authors confirmed better bowel and bladder function with lower-level resections. No change between the preoperative status and the six-month postoperative follow-up was observed. Preoperative functional status was found to be a predictor of postoperative function<sup>45</sup>.



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**Allograft Reconstruction**

Infection and allograft fractures were the subject of two large Argentinean studies. In one study, infections occurred in sixty (9%) of 673 patients with massive bone allografts. Tibial allografts, male sex, procedures performed in a conventional operating room, and prolonged use of postoperative antibiotics were found to be factors associated with infection. Forty-nine (82%) of the sixty infections eventually required the allograft to be removed. The authors placed cement spacers temporarily before subsequent reconstruction. Fourteen (34%) of the forty-one patients who underwent reconstruction eventually had failure due to reinfection. The authors advocated for salvage with an endoprosthesis<sup>46</sup>.

The other study reviewed the management of intercalary allograft fractures of the lower limb. One hundred and thirty-five cases with at least 1 cm of epiphysis remaining to allow for an intercalary allograft were included. Nineteen fractures (14%) were found, sixteen in the femur and three in the tibia. Six of the fractures (three femoral fractures and three tibial fractures) were treated with bone autograft and internal fixation. All three tibial reconstructions healed, whereas all three femoral reconstructions failed. Sixteen patients underwent replacement of the fractured allograft with a new allograft. Five (31%) of these revisions failed and were then reconstructed with an endoprosthesis or osteoarticular allograft. The authors concluded that one should consider adding a vascularized fibular graft when revising a failed femoral allograft with a second allograft<sup>47</sup>. The same group published its experience using navigation to assist resection and allograft reconstruction. On average, navigation added thirty-five minutes to the operation. The system is accurate to less than a millimeter in most cases. The authors used commercially available navigation implants, but they had also developed their own software<sup>48</sup>.

Hemicortical resection of bone tumors can be safely employed in some cortically based tumors (parosteal osteosarcoma, adamantinoma). Hemicortical allograft reconstruction of the remaining defect was reported using a nationwide Dutch sarcoma database, which included 111 patients. The authors reported excellent durability, with host bone fracture being the most common complication at 18% (twenty patients). All of the host bone fractures healed without having to remove the hemicortical allograft. The authors recommended the use of hemicortical resections with allograft reconstructions for low-grade to intermediate-grade tumors and cautioned that complication rates increased as more bone was removed<sup>49</sup>.

Karim et al. reported the benefits of reconstructing either a portion or the entire pubis after Type-III hemipelvectomies in eleven patients with follow-up of at least one year. The reported benefits include prevention of hernias and instability in the hip, particularly in resections including part of the acetabulum<sup>50</sup>.

**Endoprosthetic Reconstruction**

A study from the University of California Los Angeles (UCLA) compared oxygen consumption as a surrogate for walking ef-

ficiency, knee flexion-extension strength (measured with a dynamometer), and activity level (measured with a pedometer) in seven patients with proximal femoral reconstructions, nine patients with distal femoral reconstructions, and eight patients with proximal tibial reconstructions. These patients were compared with eight healthy controls. There was no difference in walking efficiency and activity between groups. Proximal tibial reconstructions were associated with weaker knee flexion-extension. That study provided useful information to patients about what their function may be like over time after a megaprosthesis<sup>51</sup>.

A series of studies assessed prosthesis survival and complications. Comparative studies to determine which one is better still are needed. Wafa et al. reported on total humeral endoprostheses in thirty-four adult patients. The cumulative survival at ten years was 90%. The mean Musculoskeletal Tumor Society (MSTS) score was 28 points. Infection and proximal humeral migration were the most common complications<sup>52</sup>.

Capanna et al. evaluated 278 consecutive patients reconstructed with the Megasytem C lower-limb megaprosthesis (LINK). Two hundred patients had a complete two-year follow-up. The survival rate was 75.9% at five years and 66.2% at ten years, excluding type-5 failures (tumor recurrence). There were seventy-one failures in fifty-eight implants (29%), and 59.2% of them were mechanical. The prevalence of infection was 9.5%<sup>53</sup>.

The survival and outcomes of the GMRS system (Stryker) for endoprosthetic reconstruction around the knee were reported by Pala et al.<sup>54</sup>. The overall failure rate was 29% in 247 rotating hinged prostheses. Infection was the most common cause of failure. The mean MSTS score was 84 points, with no difference between the proximal tibial replacements and the distal femoral replacements<sup>54</sup>.

Sevelde et al. reported outcomes in fifty patients with primary malignant bone tumors treated with total femoral replacements. Ten patients had an expandable prosthesis. The five-year revision-free survival of conventional total femoral replacements was 48%. The most common mechanism of failure was soft-tissue insufficiency<sup>55</sup>.

Compressive endoprostheses take advantage of Wolff's law, which stipulates that bone will adapt to the stress placed on it. A series of eighteen cases of endoprosthetic femoral reconstruction was reported, with sixteen cases having five-year survival. The two failures occurred within thirty months of the initial surgical procedure. Prostheses appear to remain stable over time<sup>56</sup>.

Prosthetic reconstruction of the proximal part of the tibia in children is challenging as it requires resection of both the distal femoral and the proximal tibial growth plate. In younger patients, it can be difficult to match the anatomy of the remaining distal part of the femur with osteoarticular allografts. The Rizzoli Orthopaedic Institute began reconstructing the proximal part of the tibia with an allograft-prosthetic composite, sparing the distal femoral physis. Limb-length

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discrepancy was the most common complication, but the mean discrepancy was 1.9 cm after contralateral epiphysiodesis. Campanacci et al. introduced this technique as an alternative to more conventional reconstructions and reported on intermediate-term follow-up<sup>57</sup>.

### Other Reconstructions

Pet et al. reported the results of a retrospective study in amputees involving targeted nerve implantation, a procedure that can decrease neuroma formation. Twelve patients had primary targeted nerve implantations and twenty-three patients had secondary targeted nerve implantations. At a mean follow-up of twenty-two months, 92% of patients who had undergone primary nerve implantation and 87% of patients who had undergone secondary nerve implantation were free of palpation-induced pain<sup>58</sup>.

The use of the claviculo pro-humeri technique for proximal humeral oncologic reconstruction was reported in four cases. This biologic reconstruction provides a stable shoulder and minimizes morbidity outside the resection bed

and also allows an early chemotherapy start. Nonunion was a problem but was manageable with vascularized grafting. Patients reported excellent MSTs scores with stable shoulders. Although this is not a new technique, the study did shine light on a pragmatic reconstructive option of which many may not have been aware<sup>59</sup>.

Santiago A. Lozano Calderón, MD, PhD<sup>1</sup>  
Kevin A. Raskin, MD<sup>1</sup>  
Francis Hornicek, MD, PhD<sup>1</sup>  
Joseph H. Schwab, MD, MS<sup>1</sup>

<sup>1</sup>Orthopaedic Oncology Service,  
Department of Orthopaedic Surgery,  
Massachusetts General Hospital,  
Harvard Medical School,  
Boston, Massachusetts

E-mail address for J.H. Schwab: jhschwab@mgh.harvard.edu

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## Update

This article was updated on January, 13, 2016, because of a previous error. The first author's last name was misspelled. Specifically, "Santiago A. Lozano Calderone" should have read "Santiago A. Lozano Calderón."