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CORR Tumor Board

CORR® Tumor Board: What are the Functional Results, Complications, and Outcomes of Using a Custom Unipolar Wrist Hemiarthroplasty for Treatment of Grade III Giant Cell Tumors of the Distal Radius?

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What are the surgical and research implications of the study, "What are the Functional Results, Complications, and Outcomes of Using a Custom Unipolar Wrist Hemiarthroplasty for Treatment of Grade III Giant Cell Tumors of the Distal Radius?" DOI: 10.1007/s11999-016-4975-0.

A Note from the Editor-in-Chief: We are pleased to present the next installment of The CORR® Tumor Board column. *The* CORR® Tumor Board *column provides multidisciplinary perspective on the themes raised in selected* CORR® *tumor papers. In this column, we will discuss the implications of the highlighted article from the varied disciplines of the Tumor Board members: Orthopaedic surgery, pathology, and radiology. This month's column features the study* "What are the Functional Results, Complications, and Outcomes of Using a Custom Unipolar Wrist Hemiarthroplasty for Treatment of Grade III Giant Cell Tumors of the Distal Radius?" *by Wang and colleagues available at:* DOI: 10.1007/s11999-016-4975-0.

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Innovation in medicine is vital to improved care for patients. However, innovation must be balanced with critical and honest assessment of outcomes, a concept pioneered in the modern era by Dr. Ernest Amory Codman. Innovations that help patients should continue in use, with adjustments and improvements, and those that do not should be abandoned or completely revised.

In orthopaedic oncology, this presents a challenge. The conditions we treat demand innovation since the alterations to the musculoskeletal system are so radical. But the diseases we treat are rare, so large, statistically valid studies are difficult (and sometimes impossible) to perform. That is why this study is so exciting. The authors developed an innovative solution to a

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challenging problem. They followed the patients in whom they used the device and formally reported their results. The authors' own assessment is honest and perhaps even overly critical. Degenerative changes of a very mild nature radiographically were counted as complications, but are very acceptable, especially when so few of these patients had any symptoms related to that. True complications were few, functional outcomes were quite good, and pain was nonexistent or mild; these results are quite encouraging for such a difficult problem.

The journal was willing to invest in this report and publish it, despite it lacking the glamour of a large study reporting positive results. There is great value in orthopaedics in accurate and fair assessment of devices, along with reporting, publishing, and reading "negative" research. We learn from our own trials and errors as well as from those of others.

What issues does this study raise in terms of musculoskeletal imaging?

Jim S. Wu MD

Musculoskeletal Radiologist

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The authors report a relatively high risk of complications among patients treated with unipolar wrist hemiarthroplasty for giant cell tumors of the distal radius. The preliminary results for this new treatment option highlight a few important considerations for the radiologist. On a practical basis, the study tells radiologists that they need to be aware of specific complications of this procedure, which include aseptic loosening, osteoarthritis, and wrist subluxation. Moreover, since some of the patients with complications were asymptomatic, imaging will likely be the first test to reveal these abnormalities, making the role of imaging even more important. From the larger perspective, the study underscores the importance for radiologists to keep up to date with new innovations being tested by our surgical colleagues as they would with the innovations we make in radiology. Although it may be hard to keep current regarding the many new kinds of implants and surgical procedures, it is our duty to do so in order to provide the best care for our patients.

What more does the surgeon need to know about musculoskeletal pathology in order to get the most out of this study?

Sara O. Vargas MD

Staff Pathologist

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While orthopedists close in on ideal surgical techniques to address giant cell tumor of bone, pathologists are making strides in diagnosing it. Classically, giant cell tumor is an epiphyseal lesion showing multinucleate giant cells evenly dispersed in a background of bland-appearing mononuclear cells. The histologic differential diagnosis with other giant-cell-rich bone lesions may become difficult when the tumor shows atypical histologic features or occurs in an unusual location. Recently, mutations in the *H3F3A* gene have been found to characterize giant cell tumor, but not other giant-cell-rich lesions [2, 4]. This finding has helped to confirm cases with unusual histologic features or metaphyseal location as bona fide giant cell tumors, expanding the clinicopathologic spectrum of the disease [1, 4]. *H3F3A* encodes a replication-independent histone (H3.3), known to have an epigenetic function regulating other genes; however, the exact mechanistic role of *H3F3A* mutation in the development of giant cell tumor is unknown. The molecular techniques to sequence the gene are not readily available in most pathology laboratories, but in difficult cases requiring diagnostic confirmation, paraffin-embedded tissue can be sent a specialized laboratory.

Although "giant cell" tumor of bone is a time-honored name, it is mononuclear cells rather than multinucleate giant cells that constitute the

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neoplasm. Mutations in *H3F3A* are confined to a subset of mononuclear cells thought to represent stromal cells. These neoplastic cells express a ligand, RANKL, which recruits numerous reactive histiocyte-like mononuclear cells bearing the corresponding receptor, RANK. In the presence of macrophage colony-stimulating factor, the reactive histocytic cells are transformed into multinucleate giant-cells. For this reason, anti-RANKL antibody (denosumab) has been introduced as a medication to restrict the growth of giant cell tumors [3].

Integration of molecular pathology into diagnosis as well as treatment rationales is an emerging field that has the potential to change the equation for surgeons as they design and implement innovative surgical therapies. In the case of giant cell tumor of bone, this impact is early and evolving—something to keep an eye on.

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