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CORR Tumor Board

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# *CORR*® Tumor Board: Is the Width of a Surgical Margin Associated with the Outcome of Disease in Patients with Peripheral Chondrosarcoma of the Pelvis? A Multicenter Study

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*What are the surgical and research implications of this study?*

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In our last *CORR*® Tumor Board column [2], we detailed the ways that advanced surgical and imaging technology integrate in the presurgical planning of pelvic and sacral sarcoma resections, how computer navigation systems can help surgeons achieve negative margins as they perform those resections, and how those margins ultimately are assessed by pathologists. The article by Tsuda and colleagues [10], makes the next logical step: Tying the quality of the margin to local and distant relapse and thus overall survival.

That study reports on a specific type of chondrosarcoma, peripheral pelvic chondrosarcomas, or what some also refer to as pelvic surface chondrosarcomas. These are uncommon tumors, about which there is limited evidence [5, 7], necessitating multicenter collaboration like that in the study by Tsuda's team [10]. They found that achieving a completely negative margin improves local control for these tumors, and pelvic chondrosarcomas can behave more aggressively clinically than their grade would suggest. Local relapse for a pelvic sarcoma can portend death in some cases, not from metastasis to vital organs, but from the pressure of large recurrences on neighboring vital organs, which diminishes overall survival.

These tumors are easy to underestimate because they appear as a somewhat dysplastic osteochondroma, but with a large cartilage cap. And while it seems straightforward simply to remove the surface of the involved bone and achieve a negative margin, these tumors often extend under the

A *note from the Editor-in-Chief: We are pleased to present the next installment of our* 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* "Is the Width of a Surgical Margin Associated with the Outcome of Disease in Patients with Peripheral Chondrosarcoma of the Pelvis? A Multicenter Study" by *Tsuda and colleagues available at:* DOI: 10.1097/CORR.0000000000000926.

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surface of the bone to invade the medullary space, making it a challenge even for very experienced teams to achieve clear margins [10]. Making matters still-more difficult, while marginal resection may be acceptable for certain low-grade surface chondrosarcomas in the appendicular skeleton, Tsuda and colleagues [10] found that this is not the case for locations in the pelvis. In this instance, the use of advanced technology, such as computer navigation and methods to more accurately show minute tumor cells in real time to guide resection and assess margins, as we discussed in our last *CORR*® Tumor Board column [2], can be invaluable. Perhaps further multi-disciplinary and multi-institutional collaboration will show that such technology not only helps to achieve negative margins, but also improves local and overall disease control for these difficult tumors, which arise in challenging locations.

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

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Determining the margins of a bone tumor can be difficult; however, as the study by Tsuda and colleagues shows [10], doing so can be a matter of life or death. Their study of pelvic surface chondrosarcomas found no tumor recurrence in patients with resection margins ≥ to 1 mm. Based on this, these authors reasonably advocate the need to achieve such a tumor-free margin. In theory, this seems simple; remove all the tumor and it will not return. However, surface chondrosarcomas arising from an osteochondroma are unique-appearing tumors—the base of the tumor blends in with the host bone making the tumor margins hard to identify on imaging. They are sessile or pedunculated osseous excrescences with a large cartilaginous cap. Much has been written about the importance of assessing the thickness of the cartilage cap on imaging, since the vast majority of these surface chondrosarcomas have a cap thickness of greater than 2 cm with the average being 5 cm to 6 cm [3, 6, 8]. Past studies have shown that measurement of the cartilage cap can be accurately performed on MRI and or CT [3, 8], and a recent study [6] suggests that quantifying the T2 relaxation time of the cartilage cap using MRI may help anticipate malignant transformation with higher T2 relaxation times, indicating more water/cellular content. However, Tsuda and colleagues [10] redirect our focus away from the cartilage cap into the medullary component of the tumor. Since the medullary cavity and cortices of osteochondromas are contiguous with the host bone, it can be difficult to determine where the tumor begins and ends. From an imaging standpoint, MRI is the best modality to determine this medullary involvement. Although there are numerous MRI sequences, the best MRI sequence for determining tumor extent remains T1-weighted sequences, where there is excellent delineation of normal fatty marrow from marrow replacing tumor. Past studies have shown that marrow edema sensitive sequences or post-contrast sequences can overestimate the degree of tumor extent in bone tumors [1, 9]. Surgeons and radiologists need to be aware of these imaging pitfalls in order to correctly identify the tumor margin. Newer computer-aided surgical navigation systems can now use MRI images, which should help in achieving tumor free margins.

Lastly, a surprising finding in the study was the low concordance (37%) between the needle biopsy and final surgical diagnoses in patients with pathology reports [10]. The diagnostic accuracy of needle biopsy for other soft tissue tumors was much higher. It would be interesting to see which areas of the tumor were targeted in the study. In our institution, if technically possible, we attempt to target enhancing nodular areas within the cartilage cap and take additional samples at the osseous base in order to improve diagnostic accuracy. Knowledge of these imaging considerations are important both for the radiologist and surgeon in order to determine the risk for malignant transformation, fully delineate tumor extent, and to identify areas to target for biopsy. For patients with complex anatomy and where determining the tumor margins is particularly challenging, the radiologist and surgeon should carefully review the images together prior to surgery in order to achieve tumor-free margins.

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

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Tsuda and colleagues [10] investigated the diagnostic concordance of biopsy and resection specimens as a component of their study by reviewing pathology reports dating back to 1983 and found that resection specimens were assigned a higher grade in a subset of patients.

The pathologic assessment of cartilaginous tumors of bone is one of the most difficult areas of pathology practice. The diagnosis and grading of central conventional chondrosarcoma of bone is prone to substantial interobserver variability [4], a problem that reflects the challenges inherent in the histologic interpretation of this tumor type. Histologic interpretation is particularly challenging because histologic features



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alone often are inadequate to assess and grade a suspected conventional chondrosarcoma, and therefore, the pathologist's sights must go beyond the view down the microscope. Multiple clinical variables such as patient age, anatomic location, pain, radiologic characteristics, and temporal evolution are integrated in the art of pathologic interpretation, adding to the degree of complexity and subjectivity involved in evaluation. From this perspective, the impressions of colleagues in orthopaedic surgery and radiology are invaluable to the pathologist. For example, enchondroma and Grade 1 chondrosarcoma can be virtually indistinguishable under the microscope; the distinction may be subjective, and so the tumor's location and clinical presentation really make a difference. Clinical features of extraosseous extension can help to favor chondrosarcoma, as can the location in the ribs, sternum, and flat bones. By contrast, location in the hands and feet favors enchondroma. If sampled, areas characterized histologically by infiltrative growth with engulfment of nonneoplastic bone can help to support an interpretation of chondrosarcoma. For Grade 2 chondrosarcomas, cellularity is increased over Grade 1 and there is modest cellular atypia with readily visualized nucleoli. Myxoid change can help confirm that a lesion merits at least a grade of 2, but this change can be patchy and may be missed in incompletely sampled tumors. Grade 3 chondrosarcoma shows still more densely arranged cells, as well as cellular pleomorphism and frank nuclear atypia. Histologically, it can be indistinguishable from a chondroblastic component of an osteosarcoma. Radiologically evident bone formation can help with this differential diagnosis.

For the above reasons and others, there are times when it is more honest for a pathologist to simply provide a differential diagnosis rather than committing to a definitive one. At my hospital, where pediatric neoplasms with unknown biologic potential often present themselves, our archives are filled with indeterminant pathology diagnoses such as: "Cartilaginous neoplasm; see Note." Multi-disciplinary evaluation by a true tumor board or similar often is helpful.

It is easy to understand why a subset of biopsy specimens would be assigned a lower grade than the resection specimen [10]. In patients whose tumors ultimately proceed to resection, the decision to resect may be taken either immediately after the biopsy result or after an interval of follow-up in which worrisome behavior is observed. The latter set of patients are a group in whom there is bias toward biopsy undergrading. Patients whose tumors are followed rather than resected after biopsy generally avert resection because of a benign, indeterminate, or low-grade diagnosis. For every patient with a low-grade diagnosis who is followed but goes to resection because of worrisome growth observed over time on imaging studies, there may be many patients with low-grade biopsy diagnoses who never have their tumors resected. If their lesions were resected, they would prove to be of low grade (concordant with the biopsy diagnosis). Such patients are not counted in studies like that of Tsuda and colleagues [10]. Either way, the resection specimen provides an opportunity for incompletely sampled lesions to reveal areas of higher-grade tumor, which is another major source of bias toward undergrading in the biopsy sample.

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