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EDITORIAL – SARCOMA

To Biopsy, or Not to Biopsy: Is There Really a Question?

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Soft tissue sarcomas (STS) represent a diverse group of histologic subtypes, each demonstrating its own unique tumor biology and propensity to recur locally or to metastasize. The retroperitoneum accounts for approximately 15–20% of all STS and about one-third of retroperitoneal masses are STS. As we have learned more about the behavior of retroperitoneal sarcomas (RPS), it has become generally accepted that histologic subtype and grade should determine the treatment algorithm and operative extent. Historically, an open surgical incisional biopsy was the approach of choice for diagnosis of suspected STS. While ensuring adequate tissue for diagnosis, this method is fraught with the potential for significant morbidity. With advances in radiology, the current standard is a percutaneous, image-guided approach. This involves a core-needle biopsy (CNB) using a 12–16 gauge needle that targets the most solid-appearing portion of a mass. A fine-needle aspiration often yields insufficient material to allow accurate diagnosis or distinguish histologic subtypes and should generally be avoided for evaluating a possible STS. The rare example of when a preoperative biopsy may not be warranted is in the example of a well-differentiated liposarcoma (WDLPS) that often demonstrates a characteristic homogeneous fat-dense appearance. However, in light of the recent findings from the European Organization for Research and Treatment of Cancer (EORTC) phase III trial ('STRASS'), the trend in potential benefit of preoperative radiation for WDLPS would necessitate a preoperative biopsy in order to confirm the diagnosis prior to considering neoadjuvant treatment.[1]

A percutaneous approach to biopsy any solid tumor hypothetically has associated risks with regard to immediate periprocedural complications, and more long-term concerns regarding needle-track seeding (NTS). Risks associated with NTS for RPS differ from those for extremity sarcoma as, for the latter, the biopsy track is often aligned with the planned incision, and/or separately excised at the time of surgery. In this issue of *Annals of Surgical Oncology*, Berger-Richardson and colleagues from the Universities of Toronto and Ottawa report early and late complications in 314 patients undergoing 358 CNBs of suspected RPS.[2] Utilizing data from each institution's prospective databases, the authors astutely included all patients with suspected RPS, which ultimately included both benign and malignant entities. Early complications were considered procedure-related (i.e. bleeding, pain, unplanned admission, pneumothorax) and were identified in 11 patients (3.1%). Identification of NTS was based on a detailed radiographic review of all patients with a local recurrence in reference to needle tract trajectory used during percutaneous biopsy. With a median follow-up of 44 months, evidence of NTS was identified in only one of 203 patients (0.5%) undergoing CNB and subsequent resection for confirmed RPS (excluding other diagnoses).

This study provides a comprehensive analysis of the risks associated with CNB in a population of patients that most accurately reflects real-world patients with both benign and malignant tumors. These data provide important information that can be used to better educate our patients on the procedure-related expectations, as well as the long-term oncologic consequences of NTS. The authors appropriately acknowledge the limitation of retrospective study of early complications and the likely underestimation of these risks. While significant complications requiring

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hospital admission and/or administration of blood products would likely be identified, the identification of more subtle, yet important risks for patients, such as periprocedural pain, would be much more difficult. Prospective study of patient-reported outcomes would be a method to more accurately determine the rates of these early complications.

The data reported in this study are consistent with previous reports. Wilkinson and colleagues reported oncologic outcomes following preoperative CNB in patients undergoing resection of an intermediate- or high-grade primary RPS at the Royal Marsden NHS Foundation Trust.[3] Of the 90 patients analyzed retrospectively, one patient developed a rectus sheath hematoma requiring hospital admission and no patients developed NTS. More recently, van Houdt and colleagues reported combined outcomes from the Royal Marsden NHS Foundation Trust and The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital following preoperative CNB in 255 patients undergoing resection of primary RPS.[4] Five patients (2%) developed NTS, of whom three had grade 2 leiomyosarcoma (LMS) and two had grade 3 liposarcoma. When compared with those patients who did not undergo preoperative CNB, there was no difference in local recurrence-free survival rates ($p = 0.3$). Similarly, there was no difference in local recurrence-free survival rates when comparing the trans-abdominal versus trans-retroperitoneal route ($p = 0.72$). No complication data were reported in this series.

While data from the current study demonstrate a low risk of both early and late complications, an important factor to consider in the discussion is the accuracy of histologic diagnosis from CNB compared with the final surgical specimen. Accuracy of diagnosis from CNB has been previously reported in 530 patients with suspected STS at various anatomic sites.[5] Benign masses versus STS were differentiated with an accuracy of 98%, and histologic subtype of STS was accurately identified in 88% of patients. High- versus low-grade STS were differentiated with an accuracy of 86%. Grade determined using the French Federation of Cancer Centers grading system is based on the assessment of tumor differentiation, mitotic count, and presence or absence of tumor necrosis. Accurate grading may be challenging, particularly in the assessment of necrosis due to heterogeneity within the tumor. This is particularly true for tumors of smooth muscle origin, with grading accuracy based on CNB reported to be only 68% in a series of 100 patients undergoing resection of LMS.[6] Of the patients with discordant grading, 45% were upgraded from low grade on CNB to high grade on the surgical specimen.

Discrepancy in grading has significant implications, not only with regard to management and prognostic consequences but also in clinical trial development. While the original STRASS trial focused on local recurrence rates, the STRASS 2 trial is currently under development with the aim of improving distant metastases rates. Patients with resectable grade 3 dedifferentiated liposarcoma (DDLPS) and grade 2–3 LMS will be randomized to surgery with or without preoperative chemotherapy (doxorubicin and ifosfamide for DDLPS, or doxorubicin and dacarbazine for LMS). In order to address potential discrepancy on preoperative CNB, grade 2 tumors with no necrosis on biopsy will be included if necrosis is present on preoperative imaging or if the tumor demonstrates a high-risk gene profile as determined by CINSARC criteria.

Advances in imaging-guided biopsy techniques have undoubtedly improved the safety and diagnostic accuracy of CNB. One advancement has been with the use of a coaxial sheathed needle biopsy technique that has been previously described by the authors.[7] Of the five patients reported by van Houdt and colleagues with evidence of NTS following CNB, none underwent CNB using a coaxial sheathed needle technique.[4] Ultimately, we rely on the expertise of our sarcoma pathologists, knowing that rates of pathologic discordance from referring institutions have been reported to be as high as 24%, with 16% of cases leading to a significant change in treatment approach.[8]

We agree with the authors that CNB should be considered a routine practice in the evaluation of suspected RPS. While the appropriate extent of resection in patients with primary RPS continues to be debated, most would agree that the knowledge that has been gained through international collaboration has led to a better understanding of the inherent, histology-specific tumor biology, which should ultimately guide our surgical approach. The authors findings further our understanding of the necessity, as well as the risks and limitations, of CNB.

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