Malignant tumors in the hand are relatively uncommon; however, it is important for the orthopedic surgeon to be familiar with a wide variety of different lesions. Primary tumors of the hand include a diverse group of lesions originating from skin, soft tissues, and bone and can be generally classified into benign and malignant lesions.

Benign lesions are far more common and include soft-tissue lesions such as ganglion cysts, retinacular cysts, lipomas, schwannomas, fibromas, and bone lesions such as enchondromas, osteochondromas, and osteoid osteomas.

The approach to working up a mass must be methodical and thorough, and clinicians must have a high index of suspicion for all soft-tissue masses. Taking a detailed history, performing a physical examination and reviewing comprehensive imaging is of paramount importance because it guides the clinician to begin to differentiate malignant lesions from benign ones. Correct identification of malignant tumors with prompt and appropriate treatment may include referral to a cancer center for staging, workup, and multidisciplinary treatment. There may be devastating ramifications if the diagnosis is missed. It is therefore imperative to understand the principles of diagnosis, staging, biopsy, resection, and amputation before treating malignant tumors of the hand.

Surgical treatment of malignant tumors in the hand is complicated by the increased number of critical structures that may be in close proximity to the tumor. However, the risk of local recurrence must be balanced against the functional loss expected from the resection. Absolute treatment principles include complete resection of the tumor with negative margins. This may be done in a limb salvage technique; however, the margins should not be compromised in an attempt to save functional structures such as vessels, nerves, or tendons.

This review provides an overview of primary malignant tumors of the hand and provides a framework to understand the workup and treatment of these various conditions.
Malignant Bone Tumors

Chondrosarcoma

Chondrosarcoma is the most common primary malignant bone tumor in the hand; however, it accounts for only 2% of all cartilaginous lesions in the hand and up to 8% of chondrosarcoma tumors throughout the body.1-3 It may arise as a primary tumor or as a secondary tumor in a preexisting chondral lesion such as an enchondroma or osteochondroma or in the context of a systemic syndrome such as Maffucci syndrome or Ollier disease. These tumors typically occur in patients older than 60 years and occur in the same distribution as enchondromas: more commonly in proximal phalanges and metacarpals and less commonly in the distal phalanges or carpus.1,3

Chondrosarcomas typically present as a slow-growing, painful lesion. As such, it may be exceedingly difficult to differentiate between a benign chondral lesion and a malignant one (Table 1). Radiographs typically reveal stippled calcifications, lytic areas, poorly defined borders with cortical expansion, perforation, or destruction. MRI of the lesion is obligatory to define the scope of the lesion and to evaluate the extent of soft-tissue involvement. If there is soft-tissue extension, there must be a high index of suspicion for malignancy (Figure 1).

A well-thought-out biopsy should be done while taking into consideration any future plans for a surgical approach for wide resection or amputation. Frozen section is unreliable in this situation, but if the expert surgeon has deemed that the findings are indicative of malignancy based on clinical and radiographic appearance of the lesion, the surgeon may proceed with primary wide excision without biopsy. After confirmation of chondrosarcoma, local and systemic staging should be performed. CT of the chest is mandatory in confirmation of chondrosarcoma, local wide excision without biopsy. After the carefully planned biopsy confirms malignancy, systemic staging is indicated including chest CT and bone scan. Adjuvant chemotherapy is considered an integral part of the treatment of high-grade lesions. Historically, rates of progression for localized high-grade osteosarcoma approached 90%; however, with the addition of adjuvant chemotherapy, disease-free survival is 65% with overall survival up to 71%.9,11 Neo- adjuvant chemotherapy may also improve the resection margin and allow preservation of vital structures. This is especially essential in the hand where vital structures are in such close proximity and therefore may enable limb salvage surgery.11

Overall, the outcomes after surgical treatment of chondrosarcoma in the hand are favorable because the tumor behaves more similar to a locally aggressive lesion with limited metastatic potential. However, patients should be monitored long term for local and distant recurrence. In low-grade lesions, local recurrence may occur after intralesional treatment, which may lead to increased metastatic potential. After appropriate surgical resection of recurrent and high-grade lesions, however, metastases and death due to disease are ultimately rare.

Osteosarcoma

Osteosarcoma is the most common primary malignant bone tumor in children; however, it is only located in the hand <0.2% of the time.7 However, when osteosarcoma is located within the hand, it may be seen in middle-aged patients and can arise from a preexisting lesion such as an area of chronic radiation exposure or be associated with Paget disease.9 In general, osteosarcomas of the hand and wrist are less likely to be high grade when compared with osteosarcomas of the rest of the upper extremity and nonextremity locations and may carry an improved prognosis.7,9

Patients generally present with an enlarging, painful mass (may be rapid or slow). It is most commonly centered around the metacarpophalangeal joints in metacarpals or proximal phalanges in the hand or at the distal radius. Radiographs most often show an expansive, sclerotic lesion or a mixed lytic and sclerotic pattern. There may also be an associated soft-tissue mass (Table 1). Lower grade lesions may be well circumscribed (Figure 2), and parosteal osteogenic sarcoma generally appears as a lesion on the surface of the bone. MRI is vital to evaluate the scope of the lesion for preoperative planning.

After the carefully planned biopsy confirms malignancy, systemic staging is indicated including chest CT and bone scan. Adjuvant chemotherapy is approached 90%; however, with the addition of adjuvant chemotherapy, disease-free survival is 65% with overall survival up to 71%.9,11 Neoadjuvant chemotherapy may also improve the resection margin and allow preservation of vital structures. This is especially essential in the hand where vital structures are in close proximity and therefore may enable limb salvage surgery.11

Wide resection of osteosarcoma is vital because positive margins have been strongly associated with local recurrence, and up to 90% of patients with local recurrence of high-grade osteosarcoma ultimately die of disease.10 Definitive local treatment likely includes ray amputation if the
A tumor is located in the digit or multiple ray amputation if the tumor is in the palm. An overall 5-year survival rate of 65% to 85% has been reported in patients with localized, non-metastatic high-grade osteosarcoma of the hand and forearm after treatment with chemotherapy in conjunction with wide surgical excision. After definitive treatment, patients must be continually monitored for local and distant recurrence.

**Ewing Sarcoma**

Ewing sarcoma is more commonly present in children and adolescents, but it only rarely occurs in the hand. Ewing sarcoma has annual incidence of just less than three cases per one million people; however, only in 1.4% of those cases is the primary site the bones of the upper extremity. It is important for the clinician to recognize that the presentation of an Ewing sarcoma may mimic infection with swelling, erythema and pain, fever, and malaise. Radiographs will demonstrate a mixed lytic and sclerotic expansile lesion with associated soft-tissue involvement. When it does occur in the hand, Ewing sarcoma is most commonly found in the phalanges or metacarpals. Biopsy and immunohistochemical staining of the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Differentiating Features Between Common Malignant and Benign Tumors of the Hand</th>
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<tr>
<td>Tumor Types</td>
<td><strong>Benign Characteristics</strong></td>
</tr>
<tr>
<td>Enchondroma versus chondrosarcoma</td>
<td>• Well-circumscribed, well-defined lesion with matrix calcifications, stable in size.</td>
</tr>
<tr>
<td></td>
<td>• Usually painless.</td>
</tr>
<tr>
<td></td>
<td>• Likely incidental finding.</td>
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<td></td>
<td>• Stippled calcified matrix on radiographs.</td>
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<tr>
<td>BPOP versus osteosarcoma</td>
<td>• Can have a cartilage component.</td>
</tr>
<tr>
<td></td>
<td>• Surface lesions (does not go into medullary canal).</td>
</tr>
<tr>
<td></td>
<td>• CT scan helpful to differentiate</td>
</tr>
<tr>
<td>Lipoma versus liposarcoma</td>
<td>• Must behave as fat on MRI in all sequences (bright on T1 sequences, suppresses on fat suppression sequences).</td>
</tr>
<tr>
<td></td>
<td>• Homogeneous appearance on MRI.</td>
</tr>
<tr>
<td>Schwannoma or neurofibroma versus MPNST</td>
<td>• Schwannoma: Eccentric elliptical shape on MRI, target sign, split fat sign.</td>
</tr>
<tr>
<td></td>
<td>• Neurofibroma: fusiform enlargement of the nerve on MRI, target sign after contrast</td>
</tr>
<tr>
<td></td>
<td>• Split fat sign on T1 MRI.</td>
</tr>
<tr>
<td>Dupuytren/palmar fibromatosis versus epithelioid sarcoma</td>
<td>• Family history or diathesis of Dupuytren.</td>
</tr>
<tr>
<td></td>
<td>• Clinical examination is vital.</td>
</tr>
</tbody>
</table>

BPOP = bizarre periosteal osteochondromatous proliferation, MPNST = malignant peripheral nerve sheath tumor

Figure 1

Plain radiograph of chondrosarcoma of the proximal phalanx with stippled calcifications and lytic areas. MRI (axial inversion recovery sequence) shows poorly defined border with cortical perforation and soft-tissue involvement.
lesion show round blue cells, and cytogenetic analysis confirms the diagnosis. After the diagnosis has been made, systemic staging is required including a total body bone scan and CT scan of the chest. Bone marrow biopsy may be performed to rule out metastasis; however, in the absence of metastatic disease seen on positron emission tomography/CT, it may be of limited additional value.15

Initial treatment should consist of chemotherapy, although definitive local control of the lesion may be accomplished with wide en bloc resection or radiation or a combination of the two.16 Notable downfalls of using external beam radiation therapy in the hand, however, include stiffness, contracture, neuropathy, and postradiation sarcoma.17

Patients with nonmetastatic disease currently have a 5-year overall survival rate of up to 78% after treatment with systemic chemotherapy in conjunction with surgery or radiation therapy for local disease control.18 Patients who develop recurrence have much poorer prognoses and higher rates of mortality; therefore, primary control is of paramount importance. In combination with chemotherapy, the author’s preferred modality to achieve local control is wide excision or partial amputation. If complete hand amputation would be required to achieve local control, radiation therapy could be considered.

**Soft-Tissue Sarcomas**

### Epidemiology

There are 13 to 16,000 new soft-tissue sarcomas reported yearly in the United States; however, only approximately 15% occur in the upper extremity and only 4% arise in the hand. Previous reports have demonstrated that patients with primary soft-tissue sarcomas of the hand may have improved outcomes as compared to similar tumors in the rest of the upper extremity or body.19,20

As a whole, it is imperative to understand that in general soft-tissue sarcomas are heterogeneous, but they originate from a primitive mesenchymal origin. Therefore, this review will provide an overview of perioperative and surgical treatment and then provide a brief description of specific subtypes seen in the hand including epithelioid sarcoma, synovial sarcoma, myxofibrosarcoma, liposarcoma, rhabdomyosarcoma, and malignant peripheral nerve sheath tumor (MPNST).

**Clinical Picture and Staging**

A painless mass in the hand is the most common presenting symptom, and the clinician must discriminate between a benign and potentially malignant lesion (Table 1). Some patients, however, may observe a mass with rapid growth or skin ulceration. Soft-tissue masses should be examined for firmness, contracture, transillumination, and depth. A complete physical examination includes palpating regional lymph nodes such as epitrochlear and axillary lymph nodes. Generalized workup and treatment principles are summarized in Table 2.

Plain radiographs should routinely be used. Soft-tissue densities, calcifications,
and bone erosions may be visualized. If the clinician does not recognize the lesion as a benign one clinically, MRI of the lesion should be used not only to aid with the differential diagnosis before biopsy but also to examine the proximity to vital structures such as blood vessels, nerves, and tendons in preparation for resection.

If there is a high suspicion for malignancy, the clinician should consider referring the patient to a specialized sarcoma center for completion of the biopsy.21 This may reduce potential error associated with performing the biopsy and facilitate the analysis of the pathology specimen at a center accustomed to looking at sarcoma histology routinely. In lesions that are larger or in close proximity to vital structures, incisional biopsy or an ultrasonography-guided core needle biopsy may be considered. The incision for the biopsy must be in-line with future possible amputation/wide resection incision so that it can be later resected.

After establishing the diagnosis of malignancy, patients should be staged with chest CT to evaluate for lung metastases and axillary lymphadenopathy. For certain high-risk histologies including angiosarcoma, epithelioid sarcoma, clear cell sarcoma, and specifically rhabdomyosarcoma—sentinel lymph node biopsy should be considered to assess for lymph node metastases at the time of the primary resection even in the absence of radiographic evidence of metastasis (Table 2). If a positive sentinel node is found, lymph node dissection in the absence of other sites of disease may be considered. The American Joint Committee on Cancer staging system can be used to stage and prognosticate based on grade, size, depth, and the presence of metastases. In addition, nomograms have been created to aide clinicians and patients in understanding the risk of local recurrence and sarcoma-specific death based on age, size, status of the margins, grade, and histology.22

### General Principles of Surgical Treatment

In general, the goal of surgical treatment of soft-tissue sarcoma is curative. Achieving negative margins after surgical resection is the primary goal because it has been shown that a positive margin is a notable risk...
factor for recurrence and cannot be compensated for with the use of radiation especially in the hand.23

Wide en bloc excision is the preferred treatment of soft-tissue sarcomas in the hand. This requires that a normal, uninvolved, nonreactive cuff of tissue be excised along with excising the tumor. In the hand, this is complicated by the large number of vital structures in close proximity to the tumor. Partial hand amputation (single or multiple ray resection) may be necessary to achieve negative margins (Figure 3) depending on where the lesion is located. These types of notable resections, however, often result in functional results.24
If the lesion is located distal to the proximal interphalangeal joint, partial digit amputation may be considered; however, if the lesion is more proximal on the digit, single ray amputation is the treatment of choice. The surgeon should prioritize thumb-sparing resections or reconstruction of the thumb after amputations at the metacarpophalangeal level to optimize function.25 If the lesion is within the palm or dorsum of the hand between metacarpals, double or multiple ray resections will be required to achieve adequate margins. With single or multiple ray resections, secondary procedures may be of benefit such as collateral ligament reconstruction, tendon transfers, and nerve grafting. If the lesion is in the carpus, wide excision with structural bone grafting and arthrodesis may be performed; however, if there is contamination of the carpal tunnel, hand amputation should be strongly considered.

Soft-tissue coverage may be necessary, which can consist of skin grafting, a local tissue flap such as a fillet flap, or even free soft-tissue transfer. This may be done in conjunction with a plastics and reconstruction surgical team if appropriate.26 Outcomes after surgical resection are encouraging, with 2-year recurrence-free survival as high as 90%. Suboptimal biopsies and positive resection margins are risk factors for local disease recurrence.23 The long-term implications of local recurrence, however, are still being investigated.

**Adjuvant Treatment Strategies**

Radiation therapy may be used as a local adjuvant after surgical excision of large or high-grade lesions. Adjuvant external beam radiation or adjuvant brachytherapy may be effective for reducing local disease recurrence; however, it has not been demonstrated to have a markedly positive effect on long-term survival in the hand or extremity.27 Notable downsides of using external beam radiation in the hand include stiffness, contracture, and neuropathy.17 The decision to proceed with radiation therapy in soft-tissue sarcoma of the hand should be made in conjunction with an experienced radiation oncologist.

Treatment with chemotherapeutic agents (doxorubicin and ifosfamide) in patients with extremity sarcomas may improve disease-free survival and overall survival.28 In a Cochrane meta-analysis study looking at doxorubicin-based adjuvant chemotherapy with localized resectable soft-tissue sarcoma, chemotherapy markedly improved the overall recurrence-free survival by 6% to 10% at 10 years. However, the overall survival benefit at 10 years was only 4%, which was not statistically significant.29 Many centers consider administering chemotherapy for soft tissue sarcoma (STS) in cases of high-grade and large (>5 cm) tumors. In the hand, STS less commonly presents with such large tumors; therefore, chemotherapy may be less frequently used when compared with lower extremity STS. However, chemotherapy may also be used preoperatively to attempt to convert an unresectable lesion to a resectable one by shrinking the lesion and creating a margin from vital neurovascular structures, enabling them to be spared during the resection (Figure 4).

In general, patients should be treated by a multidisciplinary team at a cancer center in conjunction with a medical oncologist, and lesions greater than 5 cm in size should be considered for treatment with chemotherapy.

**Common Subtypes**

**Epithelioid Sarcoma**

Epithelioid sarcoma is the most commonly reported soft-tissue sarcoma in the forearm and hand.23,30 It may present as a painless nodule with possible ulceration and must be distinguished from benign lesions such as Dupuytren nodules (Table 1). Epithelioid sarcoma can spread proximally along the tendons and lymphatics. It may even progress in a
noncontiguous fashion to the skin or subcutaneous tissue, and even as skip lesions to the fascia, bone, and lymph nodes. It can also spread directly by local extension along fascial planes \(^{31}\) (Figure 5).

Because of the high risk of lymph node involvement (the rates of lymph node metastasis of 16% to 20%), \(^{32,33}\) sentinel lymph node biopsy is recommended with ensuing lymph node dissection if the sentinel node is positive. Because of the mechanism of spread of these lesions, they require particularly wide margins of excision because marginal excision results in very high rates of local and regional recurrence. \(^{30}\) The margin of excision can be judged based on the quality and type of tissue. For example, fascia is often a good barrier and can be used as a margin of resection; however, if subcutaneous tissue is involved, a larger margin of resection should be taken as subcutaneous tissue is a poor barrier.

**Synovial Sarcoma**

Synovial sarcoma is also one of the more commonly reported soft-tissue sarcomas in the hand. \(^{19,23}\) It usually occurs in proximity to joints, tendons, or bursae. Synovial sarcoma usually presents as a slow-growing, painless mass in the palm or dorsum of the hand. On plain radiographs, soft-tissue calcifications may be seen.

Synovial sarcoma can metastasize to lymph nodes in up to a 13% of patients \(^{31}\); however, this occurs late in the disease process. Therefore, sentinel lymph node biopsy is not necessarily indicated in the initial staging workup but should be considered at the time of resection if imaging or clinical examination is concerning. Patients with synovial sarcoma may benefit from high-dose chemotherapy as preoperative or postoperative adjuvant treatment (Figure 4). This may be of particular importance in high-risk pediatric cases. One recent study showed that high-risk pediatric patients with synovial sarcoma, who underwent surgery after neoadjuvant chemotherapy, had a response rate of over 50% to chemotherapy. The 3-year event-free survival in the high-risk group (tumors with incomplete surgical resection or metastases) was 74% compared with 92% in the low-risk group (tumors <5 cm with complete surgical resection), which contained some patients who were treated with surgery alone. \(^{34}\)

**Myxofibrosarcoma**

Myxofibrosarcoma had previously been categorized as a subtype of malignant fibrous histiocytoma; however, it has been reclassified and is no longer a subtype of malignant fibrous histiocytoma. It is a multinodular tumor with pleomorphic spindle cells in a myxoid stroma. Low-grade myxofibrosarcoma can often recur after surgical resection. Recurrent low-grade myxofibrosarcoma in the hand can be infiltrative and can have a tapered tail with a superficial spread along the fascia, and it can metastasize to numerous sites including lungs, bone, soft tissue, and mesentery. \(^{35}\)

In one study, previous marginal excision and diffuse fascial spread on MRI was a risk factor for increased local recurrence. The 5-year disease-free survival was 43% for low-grade tumors and 39% for high-grade tumors. Radiation was largely ineffective at improving the outcomes after positive margins or reducing recurrence after negative margins. \(^{33}\) In addition, because of the propensity for infiltrative recurrence, this sarcoma accounts for a high number of major upper limb amputations. \(^{36}\)

**Rhabdomyosarcoma**

Rhabdomyosarcoma is the most prevalent soft-tissue sarcoma in children. It accounts for 4% to 8% of all cases; however, it rarely occurs in the hand. The 5-year survival rate is greater than 70% after multimodal treatment, but patients with low-risk, localized tumors may have an even better prognosis of greater than 90%, whereas high-risk metastatic patients have a much worse outcome. \(^{37}\) Alveolar rhabdomyosarcoma can be particularly aggressive when it is located in the hand, and the prognosis may be worse than for patients with other soft-tissue sarcomas of equal size. \(^{38}\) Rhabdomyosarcoma has a tendency for proximal lymph node involvement and distant metastasis. Therefore, sentinel lymph node biopsy should be considered in cases of extremity rhabdomyosarcoma or in cases where clinical and radiologic studies have identified concerning lymph nodes. \(^{37}\)

Surgical excision remains the mainstay of treatment in conjunction with preoperative or postoperative chemotherapy and postoperative radiation. The need for a wide surgical margin in the hand is not as defined as that for typical soft-tissue sarcomas because it is radiation and chemotherapy sensitive. In addition, if surgical excision would lead to notable functional impairment, definitive radiation therapy may be considered because it has been shown to have equivalent rates of local control in the pediatric cohort. \(^{39}\)
Liposarcoma

Liposarcoma also rarely occurs the hand; however, benign lipomas are far more common. The clinician should maintain a high index of suspicion for malignancy when evaluating a lipomatous lesion because liposarcomas can resemble lipomas clinically and on physical examination (Table 1); however, they can exhibit rapid growth. On MRI, there will be increased heterogeneity and a lack of suppression on fat suppression sequences as compared to a benign lipoma. For the tumor to be categorized as benign, it must appear as fat on all sequences of MRI. Treatment of liposarcoma includes wide excision. Adjuvant therapy such as radiation or chemotherapy can be used for larger, high-grade lesions, or in metastatic disease.

Malignant Peripheral Nerve Sheath Tumor

MPNST are uncommon, aggressive, malignant tumors of neural origin. This includes neurofibrosarcoma, neurosarcoma, and malignant schwannoma. MPNST must be distinguished based on imaging from schwannomas and neurofibromas (Table 1). Treatment of localized MPNSTs is surgical excision with curative intent; however, the prognosis remains poor. MPNST may spread hematogenously or via perineural invasion; therefore, it can track proximally along the nerve. Imaging the extremity proximal to the lesion is vital to evaluate this. In 50% of cases, MPNSTs can be seen in the setting of neurofibromatosis; however, the remainder of cases arise de novo or after radiation therapy. MPNSTs have not been shown to be particularly radio- or chemo-sensitive; therefore, wide excision is the mainstay of treatment. Despite this, MPNST has a relatively poor prognosis because it can have a high rate of local recurrence and progression. The 5-year survival rate is approximately 40% and risk factors include proximal location of the tumors, age older than 60 years, size greater than 5 cm, and the presence of NF1.

Summary

It is important to distinguish benign lesions in the hand from malignant ones because the treatment varies greatly, and misdiagnosis can have devastating consequences. Once a diagnosis of a malignant tumor of the hand has been made, appropriate management may consist of treatment by a multidisciplinary team including an orthopaedic surgeon, a medical oncologist, and a radiation oncologist at a cancer center. Principles of treatment include appropriate imaging studies and biopsy to diagnose, stage, prognosticate, and ultimately plan for surgical excision. The importance of an appropriate biopsy cannot be overstated. It is vital for diagnosis, but it is also imperative to avoid any gross contamination that will ultimately affect the surgical resection of the tumor.

Whenever possible, a limb salvage excision technique should be used; however, achieving negative surgical margins is of paramount importance. In some cases, adjuvant chemotherapy and radiation therapy may be of utility, but these treatments must be administered in the context of a multidisciplinary team.

References

References printed in bold type are those published within the past 5 years.


