Metastatic Bone Disease: Diagnosis, Evaluation, and Treatment

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Metastatic bone disease is a major healthcare issue, affecting 4.9 million individuals in the United States. The cost of bone metastasis from cancer was estimated to be thirteen billion dollars per year in the United States in 2005, and the annual incident number of cancer cases in the United States is expected to double over the next fifty years. With improved medical treatment of many cancers, patients are living longer, which places them at increased risk for the development of metastatic disease. The skeleton is the third most common target of metastatic cancer and can be one of the earliest sites affected, especially in individuals with breast or prostate cancer. Ultimately, 60% to 84% of all cases of metastatic disease invade bone, and approximately 70% of patients with metastatic bone disease experience bone pain. Patients with metastatic cancer involving bone are also at increased risk for fractures, spinal cord compression, hypercalcemia, and immobility resulting in substantial medical-associated morbidities.

Current treatment options for patients with bone metastases are primarily palliative. These options consist of local therapies, systemic treatment, and analgesics. Unfortunately, osseous metastases are generally refractory to systemic therapy. Local irradiation may be sufficient, but surgical treatment is necessary for patients with a pathologic fracture and often necessary for patients with an impending pathologic fracture.

Diagnosis
Orthopaedic surgeons are often the practitioners to whom a person with musculoskeletal pain is initially referred. If plain radiographs identify a bone lesion in the symptomatic area, the orthopaedic surgeon is then faced with a dilemma of how to proceed.

Plain radiographs yield more information about a bone tumor than any other diagnostic modality. Certain basic guidelines for interpretation of plain radiographs alert the clinician to pay particular attention to the anatomic site of the bone tumor, the zone of transition between the tumor and the host bone, and the presence of any internal characteristics that may determine the nature of the matrix that the tumor produces.

Aggressive features that can be identified on a plain radiograph include a tumor of >5 cm in diameter, interruption of the cortex, periosteal reaction, and pathologic fracture. Cortical interruption with concurrent symptoms can be considered evidence of a nondisplaced pathologic fracture.

Benign bone tumors are more common in young people, whereas malignant bone tumors, especially metastatic carcinomas, are much more common in individuals who are more than forty years old. The patient's medical history should be elicited to identify any personal or family history of malignant tumors, cancer risk factors, and systemic symptoms. The physical examination is important to identify the precise area of tenderness and the presence or absence of a soft-tissue mass. If a tumor originated in bone, the soft-tissue mass should not be mobile over the bone. Neurovascular compromise is uncommon, as is distal edema.

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Laboratory tests offer some clues that may facilitate staging. The most important laboratory tests in the evaluation of an adult with a bone lesion are measurements of serum calcium, serum immunoglobulin, and prostate-specific antigen levels and the erythrocyte sedimentation rate. Hypercalcemia is not uncommon in patients with multiple myeloma or metastatic cancer, and it can be life-threatening. A serum protein electrophoresis with a monoclonal protein spike is indicative of myeloma. An elevated level of serum prostate-specific antigen is unique to prostate carcinoma. The erythrocyte sedimentation rate is a nonspecific value that is often elevated in individuals with infection, immunologic disorders, or marrow cell neoplasms such as lymphoma, Ewing sarcoma, histiocytosis, or leukemia. A pregnancy test is warranted for a woman of child-bearing age to safely allow further radiographic imaging. Correlation among the history, findings on physical examination, and findings on plain radiographs is the key to the decision-making process, and the clinician bears the ultimate responsibility for correlating these important parameters. If a primary malignant tumor is considered a possibility, referral to an orthopaedic oncologist is justified at this stage. If the correlating clinical and radiographic data indicate that the tumor is benign, observation may be chosen. If it is more probable that the tumor is malignant, a sophisticated diagnostic and staging strategy should be employed. Even the decision to perform a needle biopsy should be made judiciously by an experienced physician.

The orthopaedic surgeon should be aware that disorders other than bone tumors cause bone lesions. These include infection, stress fracture, myositis ossificans, metabolic bone disease, osteonecrosis, and synovial proliferative diseases.

Staging Studies
The chance that a solitary bone lesion is a metastatic carcinoma in an individual older than forty years of age is approximately 500 times higher than the chance that the tumor is a primary bone sarcoma.

There are at least six good reasons to conduct a staging workup prior to biopsy:
1. The tumor may be a sarcoma; thus, a staging workup could prevent an inappropriately placed biopsy site or needle trajectory.
2. There may be a site that is easier to biopsy or one that is associated with less morbidity.
3. Preoperative embolization may be needed to prevent bleeding.
4. A biopsy can be avoided if the diagnosis can be made on the basis of the laboratory analysis, such as with multiple myeloma.
5. A working diagnosis or preoperative suspicion of a primary bone tumor on the basis of imaging studies can help the surgical pathologist to make the diagnosis more accurately on frozen-section analysis when surgery is contemplated at the time of biopsy.
6. Complete imaging combined with histopathologic analysis may make it more likely for the pathologist to accurately identify the source.

The most common steps in the workup for suspected bone metastasis of unknown origin consist of a medical history; physical examination; routine laboratory analysis; plain radiography of the involved bone and chest; whole-body bone scintigraphy (bone scanning); and computed tomography of the chest, abdomen, and pelvis with oral and intravenous contrast media. Evaluation in this fashion will identify the primary site in 85% of patients with a metastatic bone tumor. Local imaging, including magnetic resonance imaging and computed tomography, of the involved site needs to be performed only if a diagnosis of primary disease (sarcoma) is under consideration. Because breast carcinoma is common and rarely presents as a metastasis of unknown primary origin to bone, it may or may not be necessary to include a mammogram in the diagnostic strategy or workup.

Positron emission tomography is an emerging technology that has a high sensitivity for identifying malignant tumors, infections, and other physiologic processes in the skeleton and soft tissues throughout the body. Its specificity, however, is low. In several studies, positron emission tomography combined with computed tomography identified the primary tumor in approximately 50% of individuals with a metastasis of previously unknown origin. Use of positron emission tomography alone (without concomitant computed tomography) decreases the specificity to 30%.

Once all of the data have been gathered, biopsy can be performed. It can be either percutaneous (needle) or open (incisional). The pros and cons of the two techniques are beyond the scope of this lecture. Nonetheless, it is imperative to make a pathologic diagnosis prior to proceeding with any further medical, surgical, or radiation treatments. Unless the patient has a known history of histologically confirmed metastasis, radiographic findings are insufficient evidence on which to base treatment when cancer is suspected.

Pitfalls in Diagnosis and Premature Surgical Intervention
Perhaps the worst medical scenario for a patient who presents with an unknown bone lesion is the “rodded” sarcoma. A typical example is that of a forty-four-year-old man who sustained a pathologic fracture while swinging a hammer (Figs. 1-A and 1-B). A lytic lesion was suggested a metastatic malignant tumor of unknown origin. The surgeon assumed the radiographic diagnosis (metastatic carcinoma) to be correct and thus scheduled surgery for that evening. The postoperative radiograph showed an antegrade locked intramedullary nail in the humerus. Material obtained from reaming during the surgery was sent to the pathology department, and one week later the surgeon was notified that the diagnosis was osteosarcoma and not metastatic carcinoma. The treatment options now became incredibly complex, not to be outdone by the likely consequences with regard to the patient’s survival and the medicolegal
issues. The problem could have been entirely eliminated, if the diagnosis had been made first. The lesson to be learned from this case is to proceed with the staging protocol described above. One should first perform a biopsy and frozen-section analysis during the surgery and not proceed with additional surgery until the diagnosis is confidently made and the best management of the problem is clear.

**Considerations in Surgical Management**

Goals of treatment of metastatic bone disease include pain relief, preservation of function, and provision of a long-lasting construct that can be used immediately. Accomplishing these goals in an environment of osteolysis and mechanical instability can be challenging. Common errors that lead to treatment failures include underestimating the life expectancy of the patient, underestimating the abnormal bone biology in pathologic defects, and undertreating current disease while not planning for future disease. Current strategies for treatment of metastatic disease have increased overall patient survival; therefore, careful consideration must be given not only to the immediate stability of the surgical construct but also to its durability. Despite some increases in survival, the shortened life span of this population makes a reoperation due to fixation failure especially undesirable.

**Effect of Life Expectancy on Fixation Options**

A clear understanding of the life expectancy of patients with metastatic bone disease can help to prevent many common fixation errors and failures. The life expectancy of patients with metastatic disease strongly influences the choice of the method of fixation of a pathologic fracture. Patients who are likely to survive for a longer duration are more likely to undergo some level of fracture-healing and also to benefit from more extensive resections and reconstructions. However, these patients are more likely to survive longer than the reconstruction was intended to last. Surgical failures occur when local disease progresses or hardware failure occurs as a result of fracture nonunion.

Some general guidelines should be followed while it is kept in mind that treatment must be individualized. The six-month survival rates associated with tumors that commonly metastasize to bone have been reported to be 98% for prostate cancer, 89% for breast cancer, 50% for lung cancer, and 51% for kidney tumors. When the orthopaedic surgeon is not equipped to estimate life expectancy and weigh the risks and benefits of reconstruction against the anticipated life span, a medical oncologist or an orthopaedic oncologist should be consulted. Predicting the length of an individual patient’s life is difficult and unreliable; therefore, it is better to assume that the patient will live longer than one anticipates.

**Role of Patient Activity Level and Expectations in Choice of Fixation Method**

A more active, mobile patient with a longer life expectancy should be considered for a more aggressive procedure that preserves a higher level of function. Longer surgical procedures with greater risks can be justified for a patient who will obtain both short and long-term benefits. It is important that the surgical
goals be explained and reiterated so that the patients and families have realistic expectations. In particular, they should be reminded that care is palliative and not curative.

**Need for Immediate Stability**
The provision of immediate structural stability and the longevity of the construct must be considered when choosing the fixation technique. A mindset toward treating normal bone that is fractured must be abandoned and replaced with an understanding of the implications of treating persistently mechanically unstable bone with large, nonregenerating defects. Customary uses of polymethylmethacrylate, autogenous bone grafts, bone-graft substitutes, and porous ingrowth implants must be reevaluated. Constructs that would never be used to treat standard (non-pathologic) traumatic fractures are the mainstay of treatment of pathologic fractures secondary to metastatic disease.

Polymethylmethacrylate is a necessary adjunct that provides immediate structural stability and increased biomechanical rigidity when combined with the use of implants. Its behavior is predictable, it does not degrade over time, it conforms to unusual tumor cavity geometry, and it allows evaluation of early construct failure due to tumor recurrence. It has been proposed that its exothermic properties also result in some local tumor necrosis. Polymethylmethacrylate should always be considered first for the filling of a large defect caused by metastatic tumor osteolysis.

In stark contrast, autogenous bone graft and bone-graft substitutes should rarely be used. Autogenous bone graft causes donor site morbidity and pain, which is not justified in this patient population. Also, bone grafts and bone-graft substitutes require osteointegration, which is unpredictable in the setting of tumor osteolysis. Equally important is the fact that, while integrating into the defect, the construct does not allow unrestricted weight-bearing, which negates the important concept of immediate use.

**Reasons to Not Plan for Bone Ingrowth**
Another discordant concept is the use of bone-ingrowth prostheses rather than cemented prostheses in this population. Non-weight-bearing is commonly required for osteointegration of porous ingrowth implants. This may not be acceptable for a debilitated patient, who may also have upper-extremity disease precluding weight-bearing. In addition, the use of a porous ingrowth prosthesis at a site of microscopic residual disease is not recommended as the residual tumor can cause rapid loosening. One must also consider the possibility that postoperative radiation therapy contributes to bone necrosis and may lead to peri-implant failure.

**Differences Between Pathologic and Conventional Traumatic Fractures**
In order to treat metastatic bone disease the surgeon must have a solid grasp of the biology of metastatic tumors and understand how it differs from that of normal bone that is fractured. Fracture-healing rates in association with lesions that commonly metastasize to bone vary widely, with reported prevalences of 37% for breast cancer, 0% for lung cancer, 44% for kidney tumors, and 67% for myelomas. A life expectancy of longer than six months is the most positive factor predicting fracture union. A knowledge of fracture-healing rates in particular settings may affect the choice of fixation device; e.g., a distal femoral tumor with a pathologic fracture resulting from metastatic lung cancer may be better treated with a megaprosthesis, whereas a lesion from a myeloma may be amenable to open reduction and internal fixation with a plate and polymethylmethacrylate.
Understanding how aggressively a metastatic tumor needs to be treated helps in determining the appropriate degree of resection and reconstruction. The resections used to treat metastatic disease are most commonly intraleisional. Intraleisional resection leaves a large defect as well as microscopic (and sometimes macroscopic) disease that requires radiation therapy. The resection increases the size of the defect caused by the destructive tumor, and this defect requires a large, immediately structurally stable void-filler as bone will not traverse a large defect, which consequently will not heal. Expecting a large defect to heal is a common mistake that leads to a high failure rate. Treatment of massive defects can require innovative and unconventional reconstruction solutions—e.g., shortening of the bone with intercalary resection to achieve immediate bone apposition and stability or, more commonly, filling of the defect with polymethylmethacrylate.

Fixation that encompasses the entire bone, when possible, is a key element in treating metastatic disease and the large defects that it produces. Not only does it increase the mechanical stability of a construct that includes a large defect, it may also provide prophylaxis against future disease. The disease that presents in the future may arise from separate hematogenous deposits, or it may have been spread along the medullary canal when a nail was inserted through a site of macroscopic disease.

Role of Postoperative Radiation

Postoperative external beam radiation is necessary in most cases to obliterate residual microscopic disease and thus prevent disease progression and further osteolysis19. However, it also affects the bone’s blood supply, which can lead to postradiation necrosis. Postoperative radiation should include the entire operative field, which usually encompasses the entire bone20. Patients should be followed for the remainder of their lives to identify any postradiation necrosis at the tumor site as well as in the adjacent joints. Necrosis in these locations may require further treatment such as resection of necrotic bone and reconstruction with a prosthesis.

Fixation Specific to Tumor Location

Just as each patient requires individualized treatment, each osseous location requires special consideration with regard to the best type of fracture fixation. In general, pathologic fractures resulting from metastatic disease are treated by...
repairing or removing existing bone. When there is enough remaining bone with structural integrity, it may be used to anchor a nail or a plate augmented with polymethylmethacrylate. When the host bone is mechanically incompetent, there is massive bone loss, or a joint surface is destroyed, bone is removed and replaced with a prosthesis.

Although there is agreement regarding the indications for most fixation methods, there is some controversy about the best treatment for metastatic bone disease. Controversial areas include the humeral diaphysis, the acetabulum, and the femoral neck. Some treatments are chosen solely on the basis of the surgeon’s preference, whereas others are selected on the basis of experience combined with scientific principles. The principles previously described in this paper must be adhered to in order to treat any metastatic lesion optimally. In addition to predicting the patient’s life expectancy and understanding tumor biology, one must be aware of the different biomechanical properties of the different areas of the same bone to achieve the best outcomes.

The humeral diaphysis may be fixed with an intramedullary nail or a combination of a plate and polymethylmethacrylate. Although intramedullary nailing provides whole-bone fixation, it does not allow tumor debulking unless the tumor is exposed through a separate incision. It may be important to debulk a tumor that is not radiosensitive, such as a renal cell carcinoma. In cases in which debulking is planned, the tumor is usually exposed well enough for plate fixation, another reason why open reduction and internal fixation is a logical decision. Open reduction and internal fixation with a plate combined with use of polymethylmethacrylate allows additional biomechanical fixation as well as reduction and control of less radiosensitive tumors. Biomechanically, a combination of plate and polymethylmethacrylate fixation is superior to intramedullary nail fixation.

Reconstruction of periacetabular defects requires a stable construct that distributes weight from the lower extremity to the remaining pelvis and spine. This may be accomplished with use of a standard reconstruction cup, an antiprotrusio cage, polymethylmethacrylate, or polymethylmethacrylate with screw augmentation as described by Harrington. According to Harrington, the size of the construct that should be used to treat a periacetabular lesion increases as the size of the lytic defect increases. Lesions that do not breach the joint may be treated with screws or pins and polymethylmethacrylate alone (Figs. 2-A and 2-B), whereas a larger defect is better treated with an antiprotrusio cage that bypasses the lytic zone and rests on solid host bone.
Minimally Invasive Treatment of Bone Metastases

Radiation therapy, usually external beam radiation, remains the standard of care for patients with localized bone pain but no impending risk of fracture. Recently, clinicians have begun to explore alternative strategies for the treatment of osseous metastases.

Minimally invasive procedures are excellent options for the treatment of skeletal metastases in patients who are otherwise poor surgical candidates because of their age, comorbidities, or the extent of their disease. In addition, patients in whom bone metastases are refractory to radiation therapy are excellent candidates for these minimally invasive procedures.

Radiofrequency Ablation

The aim of radiofrequency ablation is to ablate tumors as widely as possible but not beyond the outer margin of the tumor. To achieve this, an electrode, which is essentially an uninsulated length of wire that acts as a monopolar emitter of energy, is inserted directly into the tumor. Alternating electric current, emitted from the tip of the electrode, heats the tissue and causes cell death due to coagulative necrosis.

Thermal diffusion progressively raises the temperature of the tissue surrounding the probe until a steady state is reached. The surrounding blood flow cools the tissue and reduces the extent of thermal coagulation.

With the patient under local anesthesia or conscious sedation, a small skin incision is made and the probe is advanced up to the farthest part of the osteolytic lesion. Once the location of the probe is confirmed with use of computed tomography or ultrasound, the electrode is advanced through the insulated needle tip. The temperature of the treated tissue as well as the skin is monitored constantly. The probe can be introduced into large lesions multiple times through additional routes, and the ablation is then extended. The use of multiple probes allows the clinician to treat larger lesions.

Radiofrequency ablation, which has been extensively studied for the...
treatment of tumors of the liver and kidney,29,31 cardiac arrhythmias32,33, unresectable pulmonary tumors34,35, and osteoid osteomas36,37, was, to our knowledge, first reported for the treatment of bone metastases by Dupuy et al. in 2000. Dupuy et al. found a significant reduction in pain in a heterogeneous population of patients. Callstrom et al.38 reported on the results of radiofrequency ablation in twelve patients with a metastatic bone lesion, measuring between 1 and 11 cm, for whom radiation therapy or chemotherapy had failed to provide symptomatic relief. On the average, the patients benefited from the treatment within one week. Four weeks after treatment, both the mean pain score and the mean score for pain interference with activities of daily living, as measured with the Brief Pain Inventory, had decreased significantly. Narcotic use was also significantly reduced.

Goetz et al.39 performed a multicenter study of percutaneous image-guided radiofrequency ablation of painful bone metastases. They reported on forty-three patients for whom the standard treatment of osseous metastases had failed or who were poor candidates for such treatment. The mean score for the worst pain before treatment, as recorded on the Brief Pain Inventory—Short Form, was 7.9 (range, 4 to 10) of a possible 10 points. Ninety-five percent of the patients experienced a significant initial decrease in pain, and the worst pain was decreased significantly at four, twelve, and twenty-four weeks.

More recently, Callstrom et al. conducted a prospective clinical trial of the use of percutaneous radiofrequency ablation guided by computed tomography and ultrasound in fourteen patients who had one or two painful osseous metastases. Each patient had a score of ≥4 points (of a possible 10) for worst pain in a twenty-four-hour period. The authors found that four weeks after treatment, the mean pain score decreased significantly, as did the mean score for pain interference with activities of daily living. All patients reported a reduction in narcotic use, and no serious complications were observed.

The mechanism by which radiofrequency ablation provides pain relief is likely multifactorial. It has been theorized that the intense heat that is generated may destroy local sensory nerves, thus effectively “numbing” the area. Also, the decrease in tumor burden (cell death) may decrease the production of cytokines and tumor factors involved both in the sensitization of the nerve endings and in the stimulus of osteoclastic activity, or the radiofrequency ablation may prevent tumor progression and thus prevent development of additional painful microfractures of the bone.

Radiofrequency ablation can provide effective palliation of localized and painful bone metastases. An additional benefit is that it can be performed on an outpatient basis. Furthermore, a biopsy, which is diagnostic in approximately 75% of cases, can be performed at the time of the procedure without decreasing or changing the structural integrity of the treated site. However, radiofrequency ablation is contraindicated when there is no safe needle access to the lesion, when there are important structures (especially nerves) within millimeters of the lesion, or when the lesions are immediately subcutaneous.

Percutaneous Cryoplasty

The use of freezing temperatures for the therapeutic destruction of tissue started in England in 1845 when James Arnott described the use of iced salt solutions to freeze certain cancerous tumors. He reported a reduction in tumor size and amelioration of pain. Improved freezing techniques were possible early in the 1990s, when solidified carbon dioxide came into use and later when liquid nitrogen and nitrous oxide became available. Currently, with the development of an argon-based system and a smaller applicator diameter, use of this technique has become more feasible at other disease sites. Like radiofrequency ablation, percutaneous cryoplasty was initially used for non-osseous lesions such as hepatic and renal tumors.40–42

As a result of the size of the probe and the lack of proper insulation, the use of first-generation devices was limited to the intraoperative setting and open procedures. However, the development of sealed cryoprobes with small diameters (1.7 and 2.4 mm) and with insulation along the shaft not only allowed the use of these devices percutaneously, but also afforded the user better control over the shape and size of the ablated area (with the use of multiple probes).

Cryoprobes are inserted percutaneously into the tissue with the patient under general anesthesia or conscious sedation. Argon gas is forced through a segmentally insulated probe. The rapid expansion of the gas results in rapid cooling, with the temperature reaching −100°C within a few seconds, and the generation of an ice ball. Active thawing of the ice ball is achieved by the instillation of helium gas, instead of argon gas, into the cryoprobe. A single cryoprobe provides an ice ball of approximately 3.5 cm in diameter. The use of multiple cryoprobes not only allows the generation of large ice balls (>8 cm in diameter), and hence the management of large lesions, but also permits the clinician to contour the shape of the ice ball. The ablation zone can be shaped by varying the geometry of the probe placement. Up to eight cryoprobes can be used independently at a time, thus decreasing the procedure time for large lesions. In addition, synchronous ablation with several cryoprobes eliminates possible residual disease at the interface of overlapping zones.

Cell death from cryoablation is due to two mechanisms: intracellular ice formation and cellular dehydration. The rapid freezing immediately adjacent to the probe results in intracellular ice formation and subsequent cell destruction; at a further distance from the probe, the gradual cooling causes osmotic differences across the cell membrane, resulting in secondary cellular dehydration and cell death.

Cryoablation treatments are more time-consuming than radiofrequency...
were treated with cryoablation. Although complete radiofrequency ablation may require several overlapping procedures, the time for each procedure is short (five to ten minutes). However, each freeze-thaw-freeze cycle of cryoablation requires twenty-five to thirty minutes and an additional ten minutes for warming prior to probe removal. An advantage of cryoablation is that the edges of the ice ball can be seen with currently available imaging. The use of cryoablation for the treatment of primary and metastatic bone lesions was, to our knowledge, first reported by Sewell et al. In their study, sixteen tumors in fourteen patients underwent cryoablation under magnetic resonance imaging guidance. They reported a reduction in pain in the postoperative period, and this reduction was apparently sustained.

Callstrom et al. reported the results of a prospective study of fourteen patients with osseous metastases that were treated with cryoablation. The lesions ranged from 1 to 11 cm in diameter. After treatment, the mean scores for the worst pain and pain interference with activities of daily living both decreased significantly. All patients who were taking narcotic pain medication reported a reduction in its use. No complications were reported. The authors concluded that percutaneous cryoablation is a safe and effective method for palliation of pain due to osseous metastases. However, they did note that they did not treat patients who were at risk for pathologic fracture, and this may have slightly skewed the results.

Cementoplasty
Percutaneous injection of polymethylmethacrylate into metastatic vertebral body lesions has been used to palliate pain. Cementoplasty is an extension of the concept of vertebroplasty. It consists of the injection of opacified bone cement into an osseous cavity, and its goals are stabilization and pain relief. Like the procedures described above, cementoplasty provides pain relief, but it has the added potential benefit of restoring the mechanical stability of the bone.

To perform the cementoplasty, a needle is hammered into the osseous lesion percutaneously under three-dimensional imaging (computed tomography or magnetic resonance imaging). Venography can then be performed to evaluate the filling pattern and identify sites of leakage. Next, the polymethylmethacrylate is injected into the cavity under continuous fluoroscopic guidance. Although complete filling of the osteolytic defect with polymethylmethacrylate is preferred, complete filling may not be necessary to confer stability. Several authors have recommended radiation of the site after the procedure to ensure local tumor control.

Serious complications include pulmonary embolus and fracture, and imaging guidance is necessary during the procedure to prevent and/or assess the leakage of the polymethylmethacrylate into the soft tissues and, in the case of acetabular lesions, into the hip joint.

Cotten et al. reported the outcomes of acetabular cementoplasty for the treatment of twelve periacetabular lesions. All patients received postoperative radiation therapy at an average of twenty-one days after the procedure. Nine of the patients had pain relief, which was sustained in all but two of them. Improvement in mobility and walking was noted within three days.

More recently, Kelekis et al. treated twenty-three lesions in fourteen patients with cementoplasty. The lesions were located in the superior and inferior pubic rami and within the ischial tuberosity. All patients had pain that was refractory to radiation and narcotic therapy. The mean duration of follow-up was nine months. The authors found that the procedure produced effective pain relief in 92% of the patients.

Cementoplasty and Radiofrequency Ablation
Although cementoplasty has been used to treat osteolytic lesions, several clinicians prefer to ablate a metastatic tumor prior to the cementoplasty. This is especially true when a bone metastasis is bulky and extends outside the bone. In such cases, cementoplasty alone may be insufficient and combination therapy can have a synergistic effect. The coagulation necrosis produced by the radiofrequency heat ablation makes homogeneous distribution of the polymethylmethacrylate in the lesion possible. The combination of the two modalities provides local tumor control, tumor necrosis, stabilization, and pain relief.

The procedure is a combination of the two techniques described above. Briefly, after the radiofrequency abla-
tion is performed, a needle is introduced into the osteolytic lesion and positioned under computed tomography guidance. The polymethylmethacrylate is then injected into the lesion under fluoroscopic guidance.

Toyota et al. treated twenty-three bone metastases in seventeen adult patients with radiofrequency ablation followed by cementoplasty. The mean tumor size was 5 cm (range, 2 to 12 cm). The technical success rate was 100%. The patients were followed for an average of two years. Initial pain relief was achieved in 100% of the patients, and the mean duration of pain relief was seven months. Three patients had recurrence of the pain from two weeks to three months after the procedure.

Nakatsuka et al. reported the outcomes of radiofrequency ablation and cementoplasty for the treatment of twenty-three metastatic bone lesions in seventeen patients. The mean tumor size was 4.9 cm (range, 1.2 to 15 cm). The procedure was technically successful in 96% of the patients. Local therapeutic effects were evaluated with contrast-enhanced magnetic resonance imaging, and tumor necrosis, indicated by a lack of tumor enhancement, was observed in 71% of the cases. Pain was relieved within one week in 100% of the patients, but it recurred in five patients at a mean of 4.9 months. The authors concluded that the combination of cementoplasty and radiofrequency ablation is a valuable treatment alternative.

Spinal Metastases

The spine is the most common site for metastatic disease, and 40% to 80% of patients with cancer have spinal metastasis at the time of death. There are approximately 18,000 new cases of spinal metastasis per year in the United States. The rate of skeletal metastases relative to that of primary bone tumors is 40:1, and skeletal metastasis must be considered in the differential diagnosis of a patient who presents with a spinal lesion.

Surgical treatment may be appropriate for spinal metastasis if there is a neurologic deficit resulting from compression by a surgically accessible lesion or if the patient has intractable pain. Surgical treatment may also be
appropriate to establish a histologic diagnosis, obtain long-term local control, address impending or actual instability, or prevent or reduce deformity. Each of these indications is related to the goals of treatment for patients with spinal metastasis, which are to protect or improve neurologic function; to interfere as little as possible with systemic treatment; to be certain of the diagnosis of the spinal lesion prior to treating it; and to reduce unrelenting pain so that the patient can return to his or her prior level of daily function, maximize mobility without using a brace if possible, and improve the quality of life in as little time as possible\textsuperscript{62-64}. The need for a histologic diagnosis warrants additional discussion. Patients with a personal history of cancer do experience spinal conditions that are not metastases, such as infections and benign tumors, just as persons without cancer do. A special situation is a spinal lesion in a patient with cancer who has not yet had a metastasis from the cancer. It behooves the treating physician to verify that the lesion is cancer prior to initiating treatment for metastatic disease, so that a benign lesion or infection, should either be present, receives the appropriate treatment. Even if a patient has established metastases elsewhere, it is appropriate to perform a biopsy to obtain specimens for pathologic analysis and microbiologic culture, prior to initiating treatment if the clinical situation, laboratory studies, and imaging studies lead to uncertainty regarding the spinal lesion in question.

The causes of pain from spinal metastases include tumor invasion of a vertebral body, pathologic vertebral fracture, spinal instability, and nerve root or spinal cord compression. Spinal instability is difficult to quantify, but there are several systems with which to classify it\textsuperscript{65,66}. Once the decision has been made that a patient is an appropriate surgical candidate, it must be established that he or she does not have any contraindications to surgery, such as impaired nutritional status, anemia, coagulopathy, hypercalcemia, too short a life expectancy, or the inability to obtain skeletal fixation if reconstruction is part of the surgical plan. Life expectancy is particularly difficult to predict, but the surgeon and medical oncologist should try to make as good an estimate as possible. We have thought that an appropriate life expectancy prior to undergoing major spinal surgery is at least three months, but this is arbitrary and varies depending on the exact clinical setting.

There are several algorithms in the literature that one can use to guide decision-making regarding patients with spinal metastatic disease. The approach described by Tomita et al.\textsuperscript{67} is a revised version of the Tokuhashi score and includes consideration of the tumor’s aggressiveness and the extent of skeletal and visceral metastases. Scores for these factors are combined to calculate a total score, which then links to treatments ranging from total en bloc tumor resection to palliative care. The system by Walker et al.\textsuperscript{68} involves a sequence of questions about neurologic deficits, stability, pain, and the tumor’s responsiveness to radiation. The answers to these questions lead to a decision regarding operative or nonoperative care. The strategies described by Tomita et al. and by Walker et al. are presented in Figures 3 and 4, respectively.

Between 1980 and 2000, there were several studies in which it was concluded that appropriate surgical decompression yielded useful improvement in neurologic function in about 80% of patients with spinal metastasis\textsuperscript{69-70}. Klimo et al. performed a meta-analysis of twenty-eight articles on the treatment of spinal metastases that had been published between 1984 and 2002\textsuperscript{71}. The data were derived from twenty-four articles in which a total of 999 patients received surgical treatment and four articles in which a total of 543 patients received radiation treatment, and the studies mostly provided Level-III evidence. Eight hundred and forty-three of the 999 patients in the surgically treated group were able to walk after the surgery, whereas only 357 of the 543 patients in the radiation-treated group were able to walk after the radiation. Of 384 patients who were unable to walk before surgical treatment, 228 regained the ability to walk after the surgery, but only seventy-nine of 265 patients who could not walk before radiation were able to do so after it. Thus, the surgically treated patients were 1.3 times more likely to be able to walk after the surgery than the radiation-treated patients were likely to walk after the radiation, and they were twice as likely to regain ambulatory function after having been unable to walk at the time that treatment began. The overall success rates with regard to the ability to walk were 84% and 66% after surgery and radiation, respectively. The authors noted that the neurologic status, overall health, extent of the disease (spinal or extraspinal), and type of primary lesion all have an impact on the appropriate treatment selection.

Patchell et al.\textsuperscript{72} reported the results of a prospective, randomized, multi-institutional nonblinded trial of patients in whom a metastatic tumor resulting in spinal cord compression was treated either with surgery followed by radiation (fifty patients) or with radiation alone (fifty-one patients). The primary end point was the ability to walk, which was achieved for significantly more patients in the surgery group (forty-two of fifty; 84%) than in the radiation group (twenty-nine of fifty-one; 57%). In addition, of sixteen patients who were unable to walk at the time that they received surgery, ten regained the ability after the surgery, whereas only three of the sixteen patients who could not walk before the radiation regained the ability after the radiation. This difference was significant. The patients in the radiation treatment arm of the study who lost their ability to walk and then had surgical decompression did not do as well as the nonambulatory patients who had surgery primarily. The patients treated with surgery retained the ability to walk significantly longer (122 days) than did those treated with radiation therapy alone (thirteen days). The rules for stopping a clinical trial were applied to this study because of the large difference in...
treatment effect between the two groups, and the conclusion was that direct decompressive surgery in addition to postoperative radiation therapy is superior to treatment with radiation therapy alone for patients with spinal cord compression caused by metastatic cancer.

The concept of performing surgical decompression first and then administering radiation was also supported by several other studies. Wise et al. addressed this issue from the perspective of complication rates in a retrospective study. They reported on eighty-eight patients who had a spinal procedure for the treatment of metastatic disease; forty-five had preoperative radiation, and forty-three did not. Six of the forty-five patients with preoperative radiation had a major complication, and ten of the forty-three had a minor complication. In comparison, four of the forty-three patients who had surgery first had a major complication and three of the forty-three had a minor complication. All of the deep wound infections in the entire series were in the patients who had had preoperative radiation.

In summary, multiple factors must be carefully considered to arrive at a treatment plan for patients who have spinal metastatic disease. One should remember that spinal metastases are common and that primary spinal tumors are uncommon, and one must be certain of the diagnosis prior to initiating treatment. When metastatic disease is present, the treatment must address the tumor cells in addition to achieving neurologic decompression and spinal column stability. The treatment recommendations from medical and radiation oncology need to be tailored to each particular patient’s clinical situation.

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