Bone Tumor Imaging, Then and Now

Review Article

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Abstract *Background:* Musculoskeletal tumor imaging is a focused subspecialty of musculoskeletal radiology. The goals of imaging and techniques employed are continually evolving and often slightly different from those used in other musculoskeletal diseases. As these techniques change, it is occasionally useful to review what is new. *Questions/Purposes:* The question addressed in this manuscript is what are the most interesting/relevant changes in each modality of musculoskeletal tumor imaging over the past 38 years, the length of time the newly emeritus chair of the Radiology and Imaging Department of Hospital for Special Surgery has been at the hospital. *Methods:* This review is primarily expert opinion based in examining techniques used at the institutions of the authors, with support from current literature. *Results:* The techniques of computed tomography (CT) and magnetic resonance imaging (MRI) are new to the imaging armamentarium, and ultrasound and nuclear medicine techniques have advanced considerably with technology. Although radiographs have also evolved, the changes are less apparent, except in how they are currently processed, viewed, and stored. *Conclusions:* Radiographic evaluation is still critical to evaluating bone tumors. Newer techniques also play an important role in diagnosing and treating these neoplasms.

Keywords bone tumor imaging · bone · tumor · radiography · CT · MRI · nuclear medicine · orthopedic oncology · imaging history

Introduction

This paper looks at advances in imaging that affect the diagnosis and treatment of orthopedic oncology, especially neoplasms of bone. As a tribute to Dr. Helene Pavlov's 38-year tenure at Hospital for Special Surgery (HSS), the article looks at changes since her arrival.

The imaging of bone tumors in the early 1970s relied heavily on radiographs. Other modalities supplemented information gained by radiographs. Bone scintigraphy (bone scans) could help stage the tumor, and angiography could help define it. There was plain tomography and fluoroscopy. Early ultrasound produced grainy images. Arthrography and myelography could show lesions in joints and the spine, respectively, but there was no way to give a three-dimensional look. Tissue characterization and staging were very basic.

Imaging now comprises a larger and more technologically advanced armamentarium that includes computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, and nuclear imaging (including positron emission tomography (PET)). With newer techniques in mind, the authors seek to answer the question, "What are the most current and interesting changes in bone tumor imaging?"

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Methods

General Pubmed searches resulted few productive results [15]. We therefore focused on specific topics of tumor imaging, such as ^{18}F PET, that we or others use in their practices in order to provide current and accurate information about those topics. This article is therefore heavily weighted toward expert opinion.

Fig. 1. Multiple familial exostoses. Multiple bony excrescences (*arrows*) around the knees cause deformity typical of multiple exostoses.

Fig. 2. Fibrous dysplasia. Child with the early finding of a “shepherd’s crook deformity,” seen in fibrous dysplasia. It forms from multiple pathologic fractures (*arrow*) which heal with deformity. Note the expansion and lucency of the left femur, involved with fibrous dysplasia.

Results and Discussion

X-rays and the Digital Format

Radiographs remain the most important imaging test for diagnosing bone tumors. They use a specific energy of photon—x-rays, which have a higher energy and shorter wavelength than visible light. Although used at HSS since 1899, major changes have taken place in their production and their viewing/storage [21].

Now, radiographs are obtained digitally—either by exposing a plate that is subsequently transferred to a digital format (CR) or directly creating an electronic image (DR). The digital images can then be electronically stored, viewed, and shared. The digital format allows easier manipulation of the image, including brightness, contrast, rotation, enlargement, and digital measurement.

Radiographs continue to allow characterization of distribution, matrix, and often aggressiveness. Many bone lesions have very characteristic appearances (e.g., Paget’s disease, osteochondromas, osteosarcoma, and fibrous dysplasia) (Figs. 1 and 2). Others have typical locations (non-ossifying fibroma, adamantinoma, and giant cell tumor of bone) (Fig. 3a). Many are more common in certain age groups (Ewing’s sarcoma and unicameral bone cyst) (Fig. 4). Other imaging techniques sometimes supplement radiographs to solve problems, define the lesion, or plan or evaluate treatment (Fig. 3) [11].

Fluoroscopy

Fluoroscopy produces real-time images on a screen using x-rays. Conventional (in distinction to CT or MRI) angiography is performed using fluoroscopy. Many use fluoroscopy to guide procedures, but it has little use in bone tumor imaging, except to localize bone tumors at the time of surgery and for angiography used in chemo-embolization treatments and preoperative embolization of vascular tumors (Fig. 5) [5, 13, 16].

Fig. 3. Giant cell tumor with aneurysmal bone cyst. In **a**, lucency goes to the end of the bone (*T*). This is a typical appearance of a giant cell tumor of bone. On the MRI with (**b**) and without (**c**) fat suppression, there is a cystic component to the lesion which contains fluid-fluid levels (*arrow*). The MRI changed the presumptive diagnosis, confirmed at biopsy, to giant cell tumor of bone with a superimposed aneurysmal bone cyst.

Fig. 4. Unicameral bone cyst. Frontal radiographs taken 1 week apart. There is a central humeral cyst (c) in this child. In **a**, a subtle fracture is present. The fracture becomes more extensive in **b** (short arrows), with a fallen fragment (long arrow) pathognomonic for a unicameral bone cyst.

Computed Tomography

CT is an x-ray technique that takes images at very thin (less than 1 mm) intervals to produce detailed information for 3-D modeling and 3-D printing. CT is useful for detailed evaluation of bone and detection of subtle calcifications, important to the differential diagnosis of tumors. Bone tumors will

also ossify as they heal, allowing CT to evaluate treatment response (Figs. 6 and 7) [18].

CT-guided procedures allow the accurate placement of needles in three planes for biopsies, even of the smallest visible lesions (Fig. 8) [19]. It also guides probes for tumoral ablation with ultrasound radiofrequency, microwave, chemical, or cryo-ablation [20].

Fig. 5. Preoperative embolization. Fluoroscopy is used in angiography show here with a catheter (arrows) in the left internal mammary artery before (a) and after (b) embolization of an aneurysmal bone cyst (T), seen on CT scan (c). Note the very vascular tumor blush (V) on the initial angiogram is very much diminished after embolization (b). The small arrow shows the small coils that were used to embolize the artery before surgery, in order to decrease blood loss from this typically vascular tumor.

Fig. 6. Treatment response. Axial CT scans of the pelvis before (a) and after (b) treatment of breast cancer metastases show sclerosis, easily detected on CT scan, which is sensitive to changes in density.

Fig. 7. Treatment response on CT. Axial CT scan of the pelvis at the level of the sacrum before (a) and after (b) denosumab treatment of a giant cell tumor of bone. Note the dense calcification from successful treatment (arrows).

Magnetic Resonance Imaging

MRI uses a strong magnet along with radiofrequency pulses to produce very detailed anatomic images of the body. MRI technology continues to advance since its introduction to clinical practice in the 1980s. MRI can be used to define, characterize, and follow tumors, as well as guide needles for diagnosis and treatment [17, 23].

After x-ray, MRI has become the primary test used to evaluate musculoskeletal tumors [3]. It is often no more helpful than the x-ray in histologic diagnosis, except in the case of certain lesions such as aneurysmal bone cysts and chondroid tumors (Figs. 3 and 9), but is able exquisitely to detail a primary tumor's extent (Fig. 10).

MRI is very sensitive to the presence of fat, to characterize lesions containing fat and to identify bone marrow

Fig. 8. CT-guided procedure. Axial CT images through the thigh show an osteoid osteoma in the femoral cortex (arrow in a). b shows a biopsy needle going into the lesion before eventual radiofrequency ablation by a different probe (c).

Fig. 9. Low grade chondral tumor. Frontal radiograph (a) and oblique coronal proton density (b) and fat-suppressed MRI (c) show the typical appearance of a chondral tumor with calcification (long white arrows). The noncalcified tumor outline (small arrows) is much more conspicuous on the MRI.

abnormalities (Fig. 10). It can be used effectively to screen the whole body for focal abnormalities/tumors such as myeloma or metastatic disease [14].

MRI has a role in evaluating response to treatment, both in size and extent of necrosis (Fig. 11) [2, 18]. Potential

exists to use MRI to distinguish certain tumors and aggressiveness based on spectral footprint, but this work has been clinically disappointing. The future holds potential for molecular markers, which can be used for tagged treatments nuclear medicine detection, and association with MRI [7].

Another role for MRI is its ability to produce angiograms. MR angiography (MRA) can evaluate blood flow to a lesion and thus the suitability of treatment with isolated limb perfusion and permits noninvasive follow-up of treatment [26].

Ultrasound

Ultrasound imaging was introduced to clinical practice in the 1960s. It is a noninvasive and inexpensive imaging modality to detect a lesion, pinpoint location, establish vascularity, and determine if it is cystic or solid (Fig. 12). Since the ultrasound beam cannot penetrate the bone, it is more useful in soft tissue lesions. However, it is effective in detecting extraosseous tumor extension and guiding biopsy or procedures.

In the past decade, image-fusion and coregistration technology have increased the power of imaging for identification of lesions and treatment guidance, as well as the potential to improve accuracy of procedures (Fig. 13). In coregistration, images can be fused into a single display [1]. Coregistration can be either simultaneous, such as in PET-CT- or MRI-guided ultrasound treatments, or nonsimultaneous [1].

Nuclear Medicine

Nuclear medicine relies on physiology and biology rather than anatomy, so-called functional imaging. Bioactive radioactive substances (radiopharmaceuticals) are injected into patients. Detection of the radioactivity can produce two- or three-dimensional images.

Typical agents used for skeletal tumor imaging include ^{99m}Tc -methylene diphosphonate (^{99m}Tc -MDP), which goes to metabolically active/forming bone and is typically used in bone scans; ^{18}F -2-fluoro-2-deoxy-D-glucose (^{18}F -FDG), which goes to areas that are actively processing glucose;

Fig. 10. Chondrosarcoma of the femur. AP view of left femur (a) demonstrates a tumor containing calcifications (arrows) and cortical thickening (arrowheads) in the distal femur. Coronal T1-weighted image (b) reveals that the tumor (arrows) is substantially larger than apparent on the x-ray, extending along the entire femoral shaft and with extraosseous mass (arrowheads). MRI (b) is superior to radiograph (A) to show the marrow and soft tissue involvement of bone tumors.

Fig. 11. Ewing's sarcoma, treatment changes. Axial MRI through the left iliac wing shows a Ewing's sarcoma (*T*). T1 (**a** and **c**) and post-contrast fat-suppressed T1 (**b** and **d**) weighted images show that after treatment (**c** and **d**), the tumor has not only become smaller, the character has changed to lack enhancement in the bone (*arrow*) and soft tissue. At surgery, the tumor had responded to chemotherapy and was 90% fibrotic.

and fluorine-18-labeled NaF (^{18}F -NaF), which mimics phosphate and is highly sensitive in detecting bone-forming processes [8].

$^{99\text{m}}\text{Tc}$ -MDP bone scan is effective in detecting bone-forming benign and malignant processes such as fractures and osteoblastic metastases (Fig. 14) and can image the entire skeleton, useful for detection of multiple lesions. However, $^{99\text{m}}\text{Tc}$ -MDP bone scan is less successful in detecting certain tumors that cause rapid bone destruction or

preventing local repair, such as thyroid metastases and multiple myeloma.

Flare phenomenon can affect $^{99\text{m}}\text{Tc}$ -MDP bone scan's assessment of tumor response to therapy. An increased uptake of the radioactive substance can be detected up to 6 months after treatment of bone metastases [6, 22]. Distinguishing flare phenomenon from disease progression is challenging and often requires additional evaluation with other imaging modalities such as MRI.

Fig. 12. Ultrasound of aneurysmal bone cyst of the sternum. **a** Transverse image of ultrasound demonstrates a sternal manubrial mass with multiple cystic foci with fluid levels (*arrows*) in a teenager patient with growing painful mass in the chest wall. The mass was initially considered as a soft tissue mass at physical exam. **b** Axial fat-saturated T2-weighted MRI confirms multiple fluid levels (*arrows*) consistent with diagnosis of an aneurysmal bone cyst. The lesion was later embolized and curetted.

Fig. 13. Screen displays of electromagnetic tracking-based ultrasound-guided biopsy of myxoma in right chest wall. **a** The real-time ultrasound (*left*) shows a heterogeneously hypoechoic mass (*arrow*) in the chest wall corresponding to the mass (*arrow*) in the reformatted post-contrast fat-saturated T1-weighted MR image (**b**). **c** The real-time ultrasound image in oblique view shows the biopsy needle (*arrowhead*) traversing the mass (*arrow*). **d** The reformatted post-contrast fat-saturated T1-weighted MR image is aligned with the ultrasound image and the mass (*arrow*) in the same orientation as the ultrasound image. (Courtesy of Majid Maybody MD).

Fig. 14. Multiple metastases and fractures at bone scan. **a** Multiple metastases from prostate cancer are evident in the axial and appendicular skeleton. **b** Multiple fractures are seen as intense radiotracer uptake (*arrows*) in the humeri, spine, ribs, pelvis, and right femur in this patient with lymphoma who is severely osteoporotic. These fractures were initially mistaken for metastases, and radiographs and CT exam (not shown) showed multiple fractures.

Fig. 15. Osseous metastatic Ewing sarcoma at PET scan and bone scan. **a** FDG uptake foci (arrows) at L2 and right superior acetabulum are present at metastases in pre treatment scan. **b** One month after chemotherapy, FDG activity is significantly decreased in metastases (arrows). Increase in FDG uptake in remainder spine and pelvis is compatible with red marrow hyperplasia. **c** Post therapy bone scan shows radiotracer uptake at L2 and right acetabulum without significant change compared to pre therapy bone scan (not shown).

The 1970s was groundbreaking for nuclear medicine, as PET technology and synthesis of ^{18}F -FDG became available [10, 24]. In 1999, a combined PET and CT scanner was introduced [4]. With advances in PET and CT technologies, ^{18}F -FDG-PET has become the dominant oncologic imaging modality in diagnosis, staging, and treatment response of primary bone tumors as well as osseous metastases. Because the metabolism of ^{18}F -FDG is similar to that of glucose, ^{18}F -FDG accumulates in malignant cells with a high glycolytic/metabolic rate. In staging, ^{18}F -FDG-PET is potentially more sensitive and specific than bone scan for detection of osseous metastases (Fig. 15) [9].

^{18}F -FDG-PET is also useful for evaluating eventual therapeutic response and detection of local recurrence. Low uptake in osteosarcoma has correlated with favorable histologic response [25]. ^{18}F -FDG-PET is less useful in evaluating body parts that normally have high uptake of the pharmaceutical, such as bowel, bladder, and bone marrow.

There has been recent interest in ^{18}F -NaF PET in tumor imaging [8]. Although the ^{18}F -NaF agent has a biodistribution similar to the $^{99\text{m}}\text{Tc}$ -MDP, there are major advantages of ^{18}F -NaF PET over $^{99\text{m}}\text{Tc}$ -MDP bone scan [12]. They include earlier image acquisition

Fig. 16. Local recurrence of parosteal osteosarcoma and lung metastasis at ^{18}F -NaF PET. **a** Axial CT image shows multiple bone-forming masses (arrows) at the left thigh. **b** Axial PET image show substantially higher radiotracer uptake in the masses (arrows), compared to the uptake in the normal right femur, and histologic diagnosis confirmed recurrent osteosarcoma. **c** Axial CT image shows a small right upper lung nodule (arrow) and post surgical pneumothoraces (asterisk) after resection of left pulmonary metastases. **d** Axial PET image demonstrates intense radiotracer uptake in the nodule consistent with a bone-forming metastasis.

(<1 h compared to 2–3 h), shorter imaging time, faster clearance of radiotracer, and higher spatial image resolution [8]. Because of high sensitivity to detection bone-forming process in skeleton and soft tissue, ^{18}F -NaF PET is potentially useful in staging and following bone-forming malignancies such as osteosarcoma and osteoblastic osseous metastases (Figs. 16 and 17) [12].

Conclusion

Radiology is an exciting field because it is technology driven and continues to change. This is also true of orthopedic tumor imaging. Each modality discussed in this paper has either come into existence or undergone remarkable changes in the past 40 years, but it is

Fig. 17. Multiple osteoblastic metastases from prostate cancer at bone scan and ^{18}F -NaF PET. **a** Bone scan demonstrates a few scattered bone metastases (*arrows*). **b** ^{18}F -NaF PET performed in the same day demonstrates a substantially larger number of osseous metastases. **c** Axial CT image and **d** axial CT-PET fusion images localize osteoblastic metastasis with tracer uptake (*arrows*) in the left transverse process of T11. (Courtesy of Neeta Pandit-Taskar MD).

perhaps because the consistent importance of the conventional radiograph that orthopedic oncologic imaging remains elegant and rewarding.

Disclosures

Conflict of Interest: Douglas Mintz, MD and Sinchun Hwang, MD have declared that they have no conflict of interest.

Human/Animal Rights: This article does not contain any studies with human or animal subjects performed by the any of the authors.

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Required Author Forms Disclosure forms provided by the authors are available with the online version of this article.

References

1. Abi-Jaoudeh N, Kruecker J, Kadoury S, et al. Multimodality image fusion-guided procedures: Technique, accuracy, and applications. *Cardiovasc Intervent Radiol*. 2012; 5: 986-998.
2. Amit P, Patro DK, Basu D, Elangovan S, Parathasarathy V. Role of dynamic MRI and clinical assessment in predicting histologic response to neoadjuvant chemotherapy in bone sarcomas. *Am J Clin Oncol*. 2013.
3. Berquist TH, Dalinka MK, Alazraki N, et al. Bone tumors. American college of radiology. ACR appropriateness criteria. *Radiology*. 2000; 215: 261-264.
4. Beyer T, Townsend D, Brun T, et al. A combined PET/CT scanner for clinical oncology. *J Nucl Med*. 2000; 8: 1369-1379.
5. Chiras J, Adem C, Vellee J, et al. Selective intra-arterial chemoembolization of pelvic and spine bone metastases. *Eur Radiol*. 2004; 14: 1774-1780.
6. Cook G, Fogelman I. The role of nuclear medicine in monitoring treatment in skeletal malignancy. *Semin Nucl Med*. 2001; 3: 206-211.
7. Costa FM, Canella C, Gasparetto E. Advanced magnetic resonance imaging techniques in the evaluation of musculoskeletal tumors. *Radiol Clin N Am*. 2011; 6: 1325-1358. vii-viii.
8. Drubach LA, Connolly SA, Palmer EL 3rd. Skeletal scintigraphy with 18F-NaF PET for the evaluation of bone pain in children. *AJR Am J Roentgenol*. 2011; 3: 713-719.
9. Franzus C, Sciuk J, Daldrup-Link H, et al. FDG-PET for detection of osseous metastases from malignant primary bone tumours: Comparison with bone scintigraphy. *Eur J Nucl Med*. 2000; 9: 1305-1311.
10. Gallagher B, Ansari A, Atkins H, et al. Radiopharmaceuticals XXVII. 18F-labeled 2-deoxy-2-fluoro-D-glucose as a radiopharmaceutical for measuring regional myocardial glucose metabolism in vivo: Tissue distribution and imaging studies in animals. *J Nucl Med*. 1977; 10: 990-996.
11. Goldman A, Schneider R, Pavlov H. Osteoid osteomas of the femoral neck: Report of four cases evaluated with isotopic bone scanning, CT, and MR imaging. *Radiology*. 1993; 1: 227-232.
12. Grant F, Fahey F, Packard A, et al. Skeletal PET with 18F-fluoride: Applying new technology to an old tracer. *J Nucl Med*. 2008; 49: 68-78.
13. Guarnieri G, Vassallo P, Muto M. Percutaneous treatment of symptomatic aneurysmal bone cyst of L5 by percutaneous injection of osteoconductive material (cerament). *J Neurointerv Surg*. Nov 2013.
14. Howe B, Johnson G, Wenger D. Current concepts in MRI of focal and diffuse malignancy of bone marrow. *Semin Musculoskelet Radiol*. 2013; 2: 137-144.
15. Hwang S, Panicek D. The evolution of musculoskeletal tumor imaging. *Radiol Clin N Am*. 2009; 47(3): 435-453.
16. Kato S, Murakami H, Minami T, et al. Preoperative embolization significantly decreases intraoperative blood loss during palliative surgery for spinal metastasis. *Orthopedics*. 2012; 9: e1389-e1395.
17. Khoo M, Saifuddin A. The role of MRI in image-guided needle biopsy of focal bone and soft tissue neoplasms. *Skelet Radiol*. 2013; 7: 905-915.
18. Manaster B, Dalinka M, Alazraki N, et al. Follow-up examinations for bone tumors, soft tissue tumors, and suspected metastasis post therapy. *Am Coll Radiol ACR Appropriateness Criteria*. 2000; 215: 379-387.
19. Mavrogenis A, Rimondi E, Rossi G, et al. CT-guided biopsy for musculoskeletal lesions. *Orthopedics*. 2013; 6: 416-418.
20. Napoli A, Anzidei M, Marincola BC, et al. MR imaging-guided focused ultrasound for treatment of bone metastasis. *Radiographics*. 2013; 6: 1555-1568.
21. Pavlov H. Radiology and imaging (1905–2012). In: Levine DB, Robbins L, Ennis M, eds. *Anatomy of a Hospital: Hospital for Special Surgery 1863–2013*. New York: Hospital for Special Surgery; 2013: 339-368.
22. Pollen J, Witztum K, Ashburn W. The flare phenomenon on radionuclide bone scan in metastatic prostate cancer. *AJR Am J Roentgenol*. 1984; 4: 773-776.
23. Sequeiros R, Fritz J, Ojala R, Carrino J. Percutaneous magnetic resonance imaging-guided bone tumor management and magnetic resonance imaging-guided bone therapy. *Radiology*. Jun 2000; 261-4.
24. Ter-Pogossian M, Phelps M, Hoffman E, et al. Positron-emission transaxial tomograph for nuclear imaging. *Radiology*. 1975; 1: 89-98.
25. Toner G, Hicks R. PET for sarcomas other than gastrointestinal stromal tumors. *Oncologist*. 2008; 13(Suppl 2): 22-26.
26. van Rijswijk C, Geirnaerd M, Hogendoorn P, et al. Dynamic contrast-enhanced MR imaging in monitoring response to isolated limb perfusion in high-grade soft tissue sarcoma: Initial results. *Eur Radiol*. 2003; 8: 1849-1858.