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Episode 1:

What are the two main varieties of bone scans in nuclear medicine?

Tc-99m-MDP (methylene diphosphate) (planar and SPECT or SPECT/CT imaging) and F18 sodium fluoride (PET imaging). Perhaps due to payment coverage of expensive PET scans, F18 sodium fluoride is less commonly used than Tc99m-MDP. A F18 sodium fluoride PET bone scan is overall more sensitive for detection of osseous metastases than a Tc99m-MDP bone scan, but also shows more uptake with reactive processes such as degenerative change with bone remodeling.

What is the critical organ for Tc-99m MDP and F18 sodium fluoride?

Remember the critical organ is the organ that will receive the highest dose from the systemic IV injection of a radiotracer. For Tc-99m MDP this is the bone itself. For F18 sodium fluoride it is the urinary bladder.

Does a bone scan show uptake more frequently in blastic or lytic osseous metastases?

Bone scans are more sensitive for, and more frequently show abnormal uptake, with blastic osseous metastases. While bone scans can also show abnormal uptake with a lytic osseous metastasis, bone scans are less sensitive for lytic metastases compared to blastic metastases. Remember that FDG-PET/CT is more sensitive for lytic osseous metastases. Therefore, neither FDG-PET/CT nor a bone scan can entirely exclude presence of osseous metastatic disease, and one exam may be preferred to the other depending on whether osseous metastases are more likely to be blastic (use MDP/NaF) or lytic (use FDG). When considering multiple myeloma, where lytic metastases are expected, both FDG-PET/CT and a radiographic bone survey will be more sensitive for disease detection compared to a bone scan.

If no renal uptake or soft tissue uptake is seen on a Tc-99m MDP bone scan, this is classic on radiology board exams for what process?

A so-called **"**superscan" denoting diffuse osseous metastatic disease. The rationale is that one should normally see soft tissue uptake (such as mild uptake in in the soft tissues of the extremities) as well as renal excretion. If neither soft tissue uptake nor renal excretion/renal uptake of radiotracer is seen, this is abnormal, and the likely mechanism is that there is so much diffuse osseous metastatic disease, and robust bone uptake (superscan named as such because bone visualized super well) that all radiotracer is going to the bone, and none is left over to be excreted by the kidneys or taken up by the soft tissue of the body. This is a highly tested concept, so it is imperative that you know how to identify a superscan. The tricky thing is that the bones can, in certain cases, look essentially normal on a superscan if the metastatic disease is truly uniform and diffuse, so in certain cases the only clue that the scan is far from normal is the lack of soft tissue and renal uptake, and lack of renal clearance of radiotracer. Other causes of a super scan are metabolic bone diseases that include hyperparathyroidism, renal osteodystrophy, and Paget's disease. A trick question can be lack of renal uptake due to renal pathology such as renal transplant (renal uptake in pelvis instead of typical bilateral upper abdomen—can confuse this for bladder or metastasis and think it is a superscan), horseshoe kidney with renal uptake about midline and lower than normal, or other renal pathologies with reduced or nearly absent renal uptake.

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What is a classic potential cause of diffusely decreased bone uptake on a Tc-99m MDP bone scan?
A primary consideration is poor tagging of Tc-99m to MDP causing poor bone localization of radiotracer. In this instance, look for signs of free Tc-99m which include salivary and thyroid uptake in the neck as well as increased gastric uptake.

If skull uptake is above normal on a bone scan, what are key differential considerations?
Renal osteodystrophy (especially if marked uptake of the cranial sutures), Paget's disease, and other metabolic bone diseases are the main considerations I would consider for a markedly hot skull on a bone scan for board exam purposes. Marked uptake of the frontal bones of an elderly patient, especially with diffuse calvarial thickening on CT, is consistent with hyperostosis frontalis. Diffuse of focal abnormal skull uptake can also be seen with metastases to the skull in the appropriate clinical setting. Uptake from inflammatory bone remodeling can also be seen in the sinuses from sinus disease, or in the maxilla or mandible from dental disease.

Besides abnormal calvarial uptake, what are additional findings of Paget's disease on a bone scan?
Additional classic findings of Paget's disease on a bone scan include a hot, expanded, and sometimes abnormally bowed femur and/or other long bone such as tibia or humerus, often flaring distally toward the knee, abnormal pelvic uptake with an expanded pelvis, which can involve only a hemi-pelvis or be more diffuse, an expanded, hot vertebral body which has been termed a "Mickey Mouse" sign as the spinous process and posterior elements can look similar to the Disney character Mickey Mouse. Finally, severe, and widespread involvement of Paget's disease can present as a super scan. The "Lincoln sign" has also been described where uptake is seen in an expanded mandible appearing perhaps like Abraham Lincoln's beard. Note that a burned-out sclerotic form of Paget's is possible in which minimal to no abnormal bone scan uptake may be seen, but as a rule Paget's is classically hot on a bone scan.

What is another classic cause of a very abnormal hot mandible on a bone scan?
Fibrous dysplasia. The most common areas of uptake with fibrous dysplasia are the ribs, femurs, and facial bones to include the mandible. Remember that the polyostotic form of fibrous dysplasia is called McCune Albright syndrome. Look for co-existing radiographs showing an expansile, often ground-glass density lesion with no periosteal reaction to confirm fibrous dysplasia.

What are classic findings of an osteoid osteoma on a bone scan?
Osteoid osteomas often appear as a double-density area of uptake with a central hot nidus within a larger area of abnormal uptake that is slightly less intense. On a three-phase bone scan, an osteoid osteoma is classically hot on all three phases. Osteoid osteomas are essentially uniformly hot on a bone scan, so a normal bone scan would essentially exclude the presence of an osteoid osteoma. Remember that osteoid osteomas are benign bone tumors most classic in children and teens that on radiography have a characteristic lucent central nidus with surrounding sclerosis. Classic clinical symptoms on a board exam stem would include pain worse or exclusively at night relieved by NSAIDs.

True or false? Aneurysmal bone cysts are classically hot on a bone scan.
True.

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How can bone scans help guide the management of heterotopic ossification?
Bone scans help show whether heterotopic ossification is mature/inactive. If bone scan uptake is present at a site of heterotopic ossification, it is not mature and you typically would not resect the area of heterotopic ossification if it is a potential surgical case. If there is no abnormal uptake, it is considered mature and therefore resectable. The key is that if you resect when heterotopic ossification is still active, this has a higher rate of recurrence/failure of surgery to clear the disease.

If a radiograph has no correlate to account for an area of abnormal or indeterminate uptake on a bone scan, does this increase or decrease the likelihood that uptake is due to malignancy?
Increases. Remember that bone scans can show osseous metastases prior to radiographic changes being present. The primary purpose of a radiograph in this setting is to evaluate for non-malignant causes of bone scan uptake, such as a subtle fracture or other benign bone lesion. If no benign radiographic cause for bone scan uptake is seen, this increases the odds that this is a metastasis because benign causes of bone scan uptake typically would show some non-malignant abnormality on an x-ray.

What is expected uptake on a bone scan for early, middle, and late phases of avascular necrosis?
Early=cold
Mid=hot
Late=cold

Early avascular necrosis does not yet have enough bone remodeling present to show abnormal bone scan uptake. Mid-phase avascular necrosis does have prominent bone remodeling from repair of AVN to result in abnormal uptake on a bone scan. Late phase AVN is essentially as repaired as it will get so there is no residual significant bone remodeling and there is classically no bone scan uptake.

Remember that causes of avascular necrosis that can clue you in to this pathology in a question stem include steroid use, alcohol use, sickle cell, pancreatitis, and trauma.

True or false? Bone infarcts classically have increased uptake on a bone scan.
False. Bone infarction, whether early or late, classically does not show abnormal bone scan uptake, at least in infarcted bone, as the bone is dead, avascular, and remodeling is not present. Note that mild uptake can be seen in the early phase in the periphery around a site of bone infarction due to bone reaction and remodeling around the necrotic bone.

What are classic bone scan findings of hypertrophic osteoarthropathy?
Linear symmetric uptake along the periosteum of the long bones, often the tibias on board exams, causing a “tram track” or “tram line” appearance. On board exams, if you see this finding first consider the possibility of a lung cancer as this is a classic association. If there is no chest imaging, this may be the next step they will test you on as you need to now exclude presence of lung cancer or other lung pathologies. Remember that hypertrophic osteoarthropathy is associated with causes of chronic hypoxia such as cyanotic heart diseases, cystic fibrosis, mesothelioma, and other cyanotic heart or lung diseases.

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Episode 2:

I need to provide a clarification on a question from the first episode regarding heterotopic ossification. I previously said that mature heterotopic ossification has no bone scan uptake, and this was too simplistic of an explanation. Mature heterotopic ossification is best evaluated by a three-phase bone scan serially to assess for a decreasing amount of blood flow and blood pool activity and delayed uptake that may either decline to a steady low level or completely resolve. The points I want to drive home are this: mature heterotopic ossification can have a persistent low-level amount of delayed uptake, or resolved delayed uptake, but importantly has resolution of hyperemia manifest by a decreased or resolved amount of blood flow and blood pool activity compared to baseline. Additionally, I want to point out that three phase bone scan is often able to detect heterotopic ossification earlier than radiographs, so can also be helpful for initial diagnosis of heterotopic ossification.

I will expand greatly our discussion of a three-phase bone scan on the next episode which will be the final episode of this three-part series on nuclear medicine bone scans.

What is flair phenomenon on a bone scan?
Flair phenomenon occurs when a patient with osseous metastases starts therapy, the metastasis reduce or resolve, the bone starts healing where the metastasis was, and increased uptake is seen on the first post-therapy bone scan. While on imaging this can look like the bone metastases are getting worse, or even new areas may be identified wherein bone at tiny, previously undetected metastases heals, but all new/increasing uptake is due to a healing response rather than worsening metastases.

How does one confirm whether increasing uptake on the first post-therapy bone scan is due to flair phenomenon or worsening disease?
The key to this answer is that one must get additional follow-up imaging to confirm flair phenomenon versus worsening metastatic disease. At follow-up 2, perhaps 2-3 months later, if uptake is now decreasing this confirms a flair phenomenon at post-therapy timepoint one. If uptake continues to worsen, this is most consistent with disease progression.

What is the classic imaging appearance of a sacral insufficiency fracture on a bone scan?
A sacral insufficiency fracture typically presents with H shaped uptake over the sacrum comprising two more laterally positioned vertical fractures and a horizontal fracture through the center of the sacrum which has been termed the Honda sign. Classic history would be an elderly female with osteoporosis with new sacral region pain.

If only one hot bone lesion is seen on a bone scan, what is the approximate percent likelihood that the solitary site of uptake is due to osseous metastatic disease?
This is a classic question for radiology board exams, and the answer is that a solitary focus of uptake has an approximate 20% likelihood of being secondary to an osseous metastasis. The exception to this rule is solitary sternal uptake in the setting of breast cancer in which the likelihood of malignancy may be greater than 50%. Some reports show that a solitary rib lesion in a person with malignancy may have up to a 40% chance of being malignant, others show a lower rate of about 10%. Ultimately, I do not like

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this question as there are many factors at play including any history of recent trauma or poor conditioning that would increase risk of fracture in clinical practice, such as a patient who has frequent falls, but for board exams, I would remember, in general, a 20% likelihood of malignancy with the exceptions I've noted.

If you see scattered areas of increased and decreased uptake through the osseous structures as well as a hot or partially hot spleen, what underlying condition should you think of first?
Sickle cell disease with variable bone uptake due to bone infarcts (remember early bone infarcts can have peripheral uptake and chronic bone infarcts have decreased/absent uptake) with additional splenic uptake caused by splenic auto-infarction. Note that sickle cell disease can also be associated with increased renal uptake.

Tc99m elution with aluminum breakthrough can cause what imaging manifestation on a bone scan?
Hepatic uptake. A potential non-metastatic cause of hepatic uptake on a bone scan is aluminum breakthrough in the Tc-99m solution. This is a must-know fact for radiology and nuclear medicine board exams.

What are classic potential causes of poor Tc-99m and MDP binding during radiopharmaceutical preparation?
Poor binding of Tc99m to MDP during radiopharmaceutical preparation can result from air in the vial or syringe during preparation causing poor binding or else not enough stannous ion in the preparation to reduce the Tc-99m which is a necessary step for Tc99m and MDP to bind. This results in imaging contamination from free Tc-99m on the bone scan which results in abnormal salivary gland, thyroid, and gastric uptake.

Beyond metastatic disease, what are 3 classic non-malignant causes of abnormal renal uptake on a bone scan?
Non-malignant causes of renal uptake on a bone scan include renal insult from nephropathy which can result from chemotherapy (can be seen on the post-treatment scans as new diffuse renal uptake) or other renal insults, as well as hemochromatosis, and urinary obstruction in which case hydronephrosis and hydroureter would also be seen.

True or false? A primary breast cancer can show abnormal breast uptake on a bone scan?
True. Soft tissue uptake in the breast on a bone scan can be a manifestation of breast cancer.

True or false? Tc99m-MDP uptake is a function of blood flow and osteoblastic activity, with binding of MDP to hydroxyapatite on the mineralizing bone surface.
True.

How long after radiotracer injection is imaging for a single-phase bone scan typically performed?
2-4 hours. For purposes of board exams, I would remember 4 hours. If a patient has renal failure, one could image after 4 hours to allow improved renal excretion which clears tracer from soft tissues, improving signal to noise.

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What is the classic imaging pattern of rib fractures on a bone scan?
Rib fractures on a bone scan classically appear as focal areas of uptake in multiple contiguous ribs in a linear pattern reflecting contiguous rib fractures at and surrounding site of impact to the ribs, often with similar uptake at all sites as all are typically the same age if from a single traumatic event.

What is the classic imaging pattern of rib metastases on a bone scan?
Scattered areas of rib uptake, often with varying intensities of uptake due to different ages of metastases, that are more diffuse than the pattern noted with rib fractures, especially if uptake is seen spreading through the marrow space of a rib rather than a focal single point. If you see uptake that follows a portion of the length or curvature of the rib, this is highly suspicious for metastatic rib involvement. If you scattered areas of rib uptake combined with suspicious bone uptake elsewhere, suspicion for rib metastases is high. Also, remember that pathologic fractures, wherein metastatic bone that is weakened undergoes a so-called pathologic fracture from minor trauma or load bearing, cannot be differentiated on a bone scan, but may be suspected, particularly if a coexisting lytic or soft tissue lesion is seen on CT or MRI imaging at the site of fracture.

What is the typical pattern for osteoporotic compression fractures of the spine on a bone scan?
Multilevel linear abnormal areas of uptake of different intensities are classic for osteoporotic compression fractures on a bone scan. Note that a single vertebral body with linear-type uptake is also consistent with a compression fracture, but whether this is pathologic or due to osteoporosis would be uncertain based off a bone scan alone. In such setting, correlating with CT or MRI can be helpful to evaluate for any underlying lesion to suggest a pathologic compression fracture. I would remember for board exams that multilevel linear areas of uptake of varying intensity are the typical pattern for multilevel osteoporotic compression fractures. These would be expected to show decreased uptake on follow-up bone scans due to healing and reduced osteoblastic activity.

If you are called by the technologist to check a bone scan prior to the patient leaving, and uptake over the pelvis is seen that is indeterminate for metastases versus urine contamination, what is the next best step?
Remove potentially contaminated clothing, clean the skin, place a clean gown, and reimage the pelvis. If the indeterminate activity goes away this confirms urine contamination. Note also that a tail-on-detector (TOD) view can also help differentiate uptake external to the pelvis from true bone metastasis.

If you see focal abnormal myocardial uptake on a bone scan, what are the primary diagnostic considerations for board exams?
I would first consider myocardial infarction with myocardial necrosis or ventricular aneurysm as possible considerations. This is also reported with unstable angina. Appropriate cardiac workup would be indicated.

If you see diffuse abnormal myocardial region uptake on a bone scan, what are the primary diagnostic considerations for board exams?
Think diffuse processes to include cardiac amyloidosis, pericarditis, chemotherapy-induced cardiotoxicity, and cardiomyopathies such as alcoholic cardiomyopathy.

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If you see diffuse increased lower-level activity throughout the abdomen, what should you first consider for board exams?
Ascites. The same principle holds true for the thorax wherein low-level diffuse symmetric or asymmetric uptake projecting over portions of the lungs, such as part of a hemithorax, can be a manifestation of pleural effusion. One should evaluate for causes of malignant ascites or pleural effusion, if not already known.

Note that soft tissue extraosseous uptake can result from abnormal blood flow, capillary permeability, or extensive calcifications in the tissues to include calcified femoral or other major arteries. Hypercalcemia and other calcium-depositing diseases can cause abnormal uptake on a bone scan. Other considerations include various malignancies whenever uptake is focal and abnormal, such as in the breast with potential breast cancer.

Episode 3

What are classic imaging findings that can be seen on a bone scan for patients who are on bisphosphonate therapy?
The first thing I would remember is a proximal femur fracture, sometimes termed a "bisphosphonate fracture" or even more specifically a "bisphosphonate-related proximal femoral fracture". On a bone scan, this would manifest as an area of focal uptake in the proximal femur that involves, often exclusively, the lateral femoral cortex of the proximal femoral diaphysis, located distal to the lesser trochanter. This can be unilateral or bilateral. Note that this is an insufficiency-type fracture and is associated with delayed fracture healing and has a risk for progression to complete fracture. When this is seen, correlation with radiographs of both femurs is often helpful, and would be predicted to show a predominantly simple horizontal fracture, classically non-comminuted. No associated mass on imaging or history of major trauma is expected in a bisphosphonate-related proximal femur fracture. Classic history would be an older woman with osteoporosis. Treatment often involves withholding further bisphosphonate therapy and surgical management to prevent completion of the fracture and promote healing.

Second, I would remember bisphosphonate-related osteonecrosis of the jaw. This is development of exposed bone with osteonecrosis in the maxillofacial region in patients on typically longer-term bisphosphonate therapy. Note that biopsy of the bone for diagnosis can worsen the process, and diagnosis is often clinical and imaging only. On a bone scan, expect abnormal, focal, often intense uptake in the jaw region. Note that bone scan is more sensitive than radiography in the early diagnosis of bisphosphonate-related osteonecrosis of the jaw.

What are key differences of physiologic uptake on a bone scan of a child or teenager compared to a physically mature adult?
Children and young adults show intense activity in the physes secondary to bone growth with associated osteoblastic, bone-building activity that is not seen in a physically mature adult. Normal physiologic uptake can also be more pronounced in children and young adults in the sternum, sacroiliac joints, articular surfaces, and nasopharynx.

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What are the three phases of a three-phase bone scan?
First is evaluation of blood flow, second is evaluation of blood pool, and third is delayed bone imaging.

In the first phase, imaging immediately following injection of the radiotracer is performed to evaluate for increased blood flow. This is a dynamic phase that usually requires positioning the patient in front of the camera first, and then immediately starting imaging at time of injection, taking images every few seconds over about 60 seconds. The second phase is blood pool, in which imaging is performed after the blood flow phase, over several minutes duration to evaluate for abnormal radiotracer accumulation in the soft tissues. Finally, about 2-4 hours after injection, delayed phase images are obtained to evaluate for abnormal radiotracer accumulation in the bone itself.

Think about the first two phases as telling you what is going on in the soft tissues around the bone in terms of infection or inflammation and the delayed phase telling you if bone pathology is present.

Often, a three-phase bone scan is performed to evaluate a clinical or imaging finding of concern, and imaging is focused over a certain region of the body only. However, it may not be unusual in cancer patients particularly to obtain the initial imaging in all three phases over a specific area of concern, and then to also get whole body delayed imaging to evaluate the entire skeleton for metastases or other abnormalities.

Finally, SPECT/CT fused images may be obtained at the area(s) of concern on delayed imaging, as clinically directed.

What are general findings of infection on a three-phase bone scan?
First, look for asymmetry. Infection or inflammation will show asymmetric uptake due to increased asymmetric blood flow and blood pool due to inflammation in the affected tissues. Infection in the bone will also show abnormal delayed radiotracer uptake on the delayed phase of imaging.

How can one differentiate cellulitis from osteomyelitis on a three-phase bone scan?
Cellulitis demonstrates increased uptake on a three-phase bone on the flow and blood pool phase but shows no abnormal uptake on the delayed phase. To explain further, cellulitis is a soft tissue infection associated with increased blood flow and inflammation in the soft tissues, but no bone involvement. Therefore, increased uptake is expected on blood flow and blood pool imaging but, importantly, not delayed imaging.

On the other hand, osteomyelitis is infection of the bone, and has inflammation of the surrounding soft tissues, and therefore is expected in classic cases to show uptake on all three phases. Remember that osteomyelitis can be detected on bone scan several days to weeks before changes will be seen on a radiograph and the sensitivity of a bone scan for osteomyelitis is something like 95%. Note that blood flow and blood pool phases should resolve within months of treatment of osteomyelitis, but abnormal bone uptake may persist for something like 2 years.

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Remember that osteomyelitis is three-phase hot on a bone scan. Cellulitis is only hot on the first two phases (i.e., blood flow and blood pool).

What are classic imaging findings of complex regional pain syndrome/reflex sympathetic dystrophy on a three-phase bone scan?
Increased blood flow and blood pool activity and delayed activity in a juxta-articular distribution, which is most classically shown in a hand on a bone scan on board exams. This is essentially an Aunt Minnie finding so make sure and look up the imaging appearance of complex regional pain syndrome on a bone scan if you don't know what this looks like. Remember that clinical symptoms of complex regional pain syndrome include pain, swelling and vasomotor instability that is often post-traumatic in etiology.

How can one differentiate orthopedic hardware infection versus loosening on a bone scan?
Infection of hardware would typically show a more generalized increase in activity around the prosthesis whereas loosening without infection would show a more localized, focal area of uptake, particularly on blood flow and blood pool imaging. This rule is not perfect but in general, expect more intense and diffuse abnormality around the prosthesis with infection, and a more localized, focal area of uptake, often around the more distal stem of a prosthesis, with aseptic loosening.

Name several abnormalities that are three-phase positive on a bone scan?
Acute fracture, osteomyelitis, complex regional pain syndrome, inflammatory arthritides, orthopedic hardware infection or loosening, aggressive and vascularized tumors, and the immature phase of myositis ossificans, and osteoid osteoma.

What are two classic entities to keep in mind on board exams for something that is only two-phase (i.e., blood flow and blood pool) positive on a bone scan?
First, consider cellulitis of the soft tissues. Second, consider a soft tissue malignancy without bone involvement.

What are classic entities to keep in mind for board exams for things that are only hot on the delayed phase of a three-phase bone scan?
When blood flow and blood pool are normal but delayed images are positive on a three-phase bone scan consider osteoblastic metastases, metabolic bone diseases, non-acute fractures, and medial tibial stress syndrome/shin splints.

What are classic findings on a bone scan for medial tibial stress syndrome/shin splints?
Longitudinal uptake along the posterior and medial aspect of the tibia, often best depicted on lateral views, with classically normal uptake on blood flow and blood pool images. Remember that if you also see early phase uptake this suggests possible stress fracture which may be acute which is a known complication of medial tibial stress syndrome if stress from running is excessive.

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If radiotracer fails to adequately clear from the soft tissues on the delayed phase of a bone scan, what classic entity should you consider first? What should you do about this?
Renal failure. Poor renal function limits the clearance of radiotracer from the soft tissues of the body. If this happens, obtain delayed imaging up to 24-hours after injection to allow more time for radiotracer to clear from the soft tissues, to improve signal to noise. Given lower counts that will be present in the body due to radiotracer decay, a longer imaging acquisition time can be helpful when extended delays in imaging are necessary.

Some refer to a delayed 24-hour imaging timepoint as the "4th phase" of a bone scan. Another scenario where a delayed 24-hour imaging timepoint may be helpful is in a neuropathic foot where peripheral blood flow may be reduced, and one needs to evaluate for cellulitis versus osteomyelitis for which radiotracer clearance from the soft tissues is helpful to improve signal-to-noise of the bone itself.