<table>
<tr><th>Authors/study design</th><th>Study Population/ Inclusion/exclusion</th><th>Procedure/outcome measures</th><th>Results</th><th>comments /Conclusions</th></tr>
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<td>Lagura et al, 2012

Study type:
Comparison of diagnostic tests.

Aim:
To compare the diagnostic accuracy of ^{18}F-NaF PET/CT versus either ^{18}F FDG PET /CT and ^{99m}Tc bone scintigraphy (BS) in the diagnosis of bone metastases from various cancer sites.

Primary outcomes:
Sensitivity, specificity, accuracy and predictive values of each test.</td>
<td>Inclusion criteria:
Patients with biopsy proven recurrent malignancy who were referred to the Nuclear Medicine Division in Stanford University Medical Center between September 2007 and December 2010, for the evaluation of possible metastases with a ^{99m}Tc MDP bone scan.

N of study population:
N= 52.

Population characteristics:
The age of the participants ranged from 19 to 84 years (average 55.6±15.9 years), 71% were men, 19 patients had sarcoma, 18 prostate cancer, 6 breast cancer, 2 colon cancer, and one of each bladder cancer, lung cancer malignant paraganglioma, renal cancer, salivary gland, lymphoma, or GI stromal tumor.</td>
<td>Procedure:
All patients were referred for evaluation of possible bone metastases with ^{99m}Tc MDP test. After enrollment they had an additional ^{18}F-NaF PET/CT ^{18}F-FDG PET/CT scans. All tests were completed in one month, and interpreted by two board certified nuclear medicine readers, and agreement was reached by consensus. A direct comparison of detected lesions was performed among the three scans.

Gold standard
Diagnostic accuracy was evaluated by comparing the results with final diagnosis confirmed by histological evaluation (n 46% of the patients), clinical follow-up (54%) of cases and other imaging studies.

Blinding:
Yes, the nuclear medicine readers who interpreted the results were blinded to the diagnosis and the results of the other imaging studies.</td>
<td>Sensitivity specificity, accuracy and predictive values for the different tests for the detection of any bone metastases
<table>
<tr><th></th><th>^{99m}Tc bone scintigraphy</th><th>^{18}NaF PET/CT</th><th>^{18}F-FDG PET/CT</th></tr>
<tr><td>Sensitivity*
Specificity*
Accuracy*
PPV (95% CI)†
NPV (95% CI)‡</td><td>87.5 (75.7-93.0)
92.9 (82.7-97.9)
90.4 (79.5-95.5)
91.3 (79.0-97.1)
89.7 (79.9-94.2)</td><td>95.8 (85.2-99.2)
92.9 (83.8-95.7)
94.2 (84.4-97.3)
92.0 (81.8-95.2)
96.3 (86.9-99.3)</td><td>66.7 (54.7-70.1)
96.4 (86.2-99.4)
82.7 (71.7-85.8)
94.1 (77.3-98.9)
77.1 (69.0-79.5)</td></tr>
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* (95% CI)
† Positive predictive value
‡ Negative predictive value
Sensitivity and specificity for the three diagnostic tests for the detection of bone metastases due to prostate cancer
<table>
<tr><th></th><th>^{99m}Tc bone scintigraphy</th><th>^{18}NaF PET/CT</th><th>^{18}F-FDG PET/CT</th></tr>
<tr><td>Sensitivity (95% CI)</td><td>87.5 (62.3-97.5)</td><td>100 (76.9-100)</td><td>55.6 (35.5-55.6</td></tr>
<tr><td>Specificity (95% CI)</td><td>80 (59.9-88.0)</td><td>80 (61.5-80.0)</td><td>100 (79.9-100)</td></tr>
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<td>The study had the advantage of including consecutive patients, all undergoing the three tests, and blinded interpretation of the tests. However, the study was small, and included patients with a variety of primary carcinomas. It had potential selection bias as all patients had biopsy proven recurrent malignancy. The gold standard used to confirm the final diagnosis of bone metastases was biopsy in 46% of cases, and clinical follow-up for the rest.
The results of the study show that overall; ^{18}NaF PET/CT is more sensitive than ^{99m}Tc bone scintigraphy and ^{18}F-FDG PET/CT in detecting bone metastases. Its specificity was lower than ^{18}F-FDG PET/CT but similar to that of the bone scan.
A subgroup analysis for patients with prostate cancer also shows that ^{18}NaF PET/CT had higher sensitivity and lower specificity than FDG-PET/CT. The latter however, had a higher specificity. These results must be interpreted with caution due to the small sample size, the selection bias and the heterogeneity of primary lesions included.</td>
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