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Opportunities and Approaches for Supplying Molybdenum-99 and Associated Medical Isotopes to Global Markets
IAEA Symposium Vienna Vienna, 2017

Establishing and Expanding Nuclear Medicine Programs

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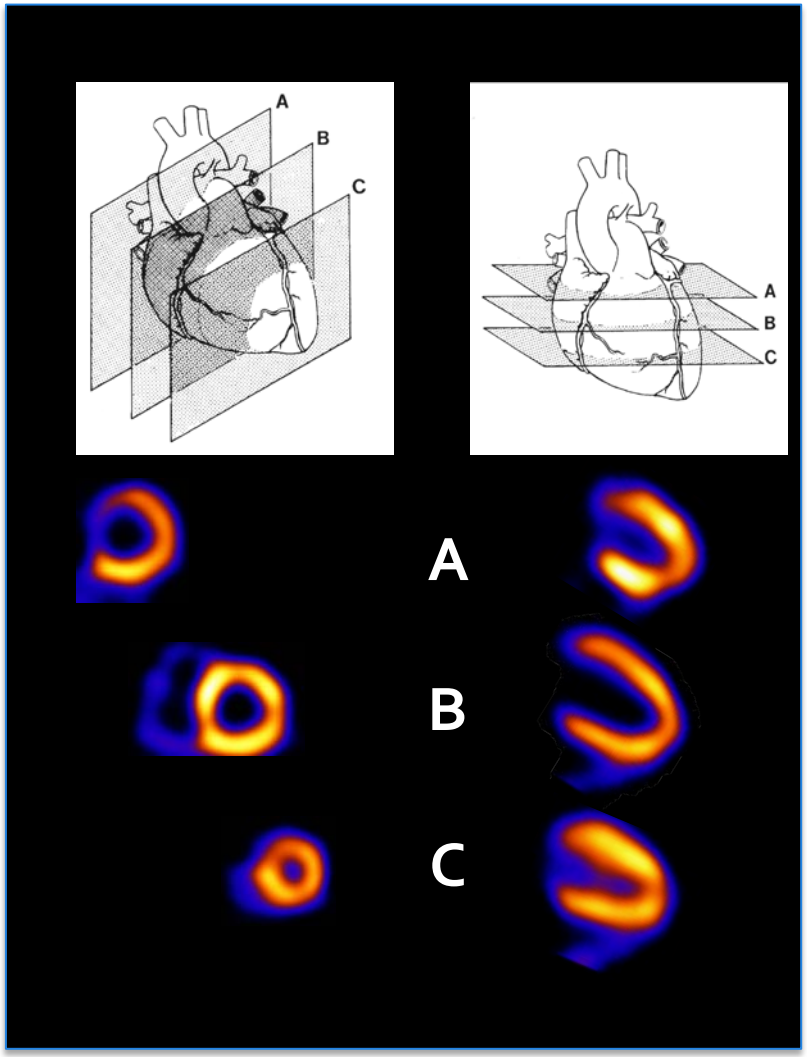
Key existing Applications of ^{99m}Technetium

Myocardial perfusion imaging for coronary artery disease (CAD)

- Decreased use in the US during the last 5 years due to changes in the reimbursement system
- Still dominates the overall demand for technetium-99m due to the high prevalence of CAD and relatively large amounts of ^{99m}Tc needed/scan
- Well established evidence supporting its use for
  - Diagnosing CAD
  - Guiding (invasive) therapies
  - Assessing prognosis



Underwood et al. Eur J Nucl Med Mol Imaging (2004) 31:261–291

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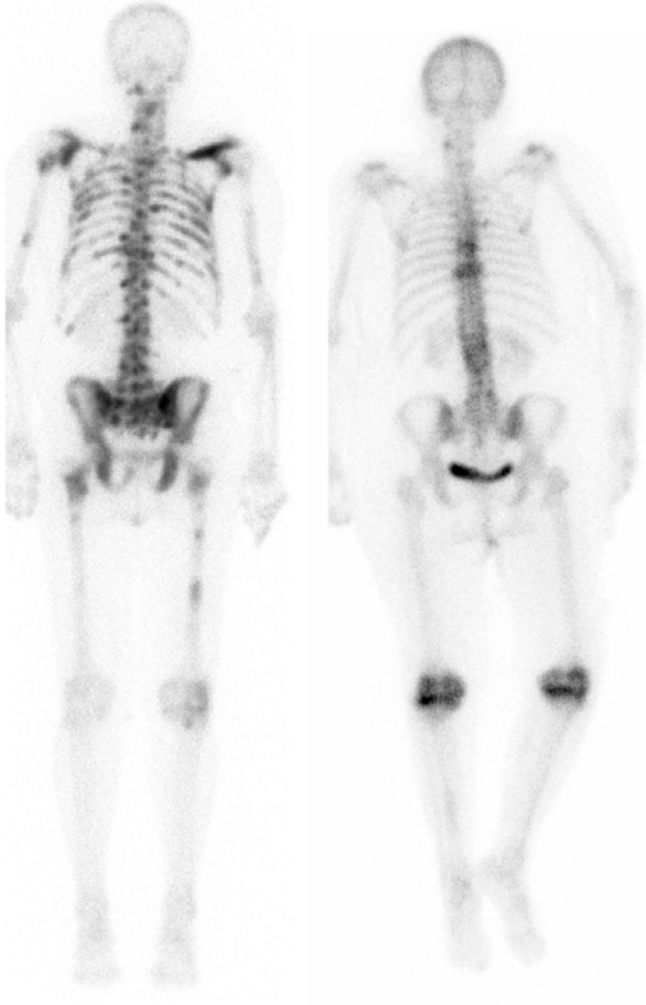
Key existing applications of ^{99m}Technetium

Bone scans

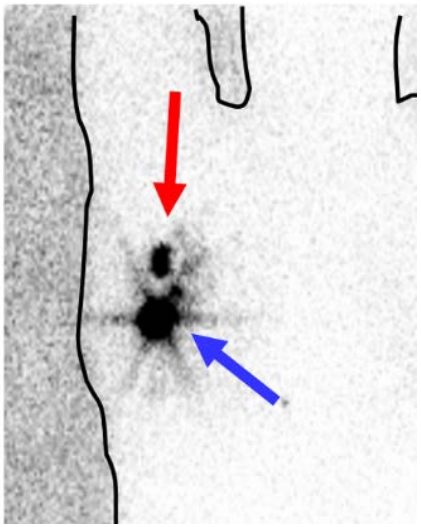
- Whole body imaging of bone metabolism
  - Detection of bone metastases
  - Several (smaller) indications in benign bone diseases, such as inflammation
- Part of international guidelines for common malignancies, including breast and prostate cancer (e.g. prostate cancer working group criteria).
- Use has decreased because of the success of FDG PET/CT for detection of bone and soft tissue metastases
- Still commonly used in international clinical trials of new pharmaceuticals

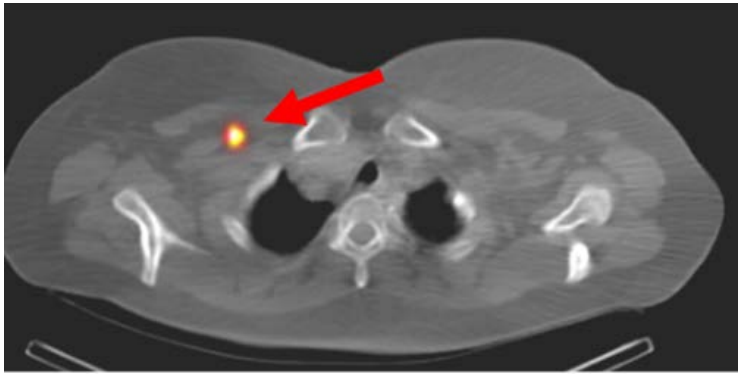


Key existing applications of ^{99m}Technetium

Other applications, less commonly used but important

- Sentinel node imaging before surgery of breast cancer, melanoma, …
- Thyroid scans
- Lung scans
- Renal scans
- Individually less commonly used than bone scans/myocardial perfusion imaging
- However, few (really) competing modalities due to simplicity and cost-effectiveness of the ^{99m}Tc





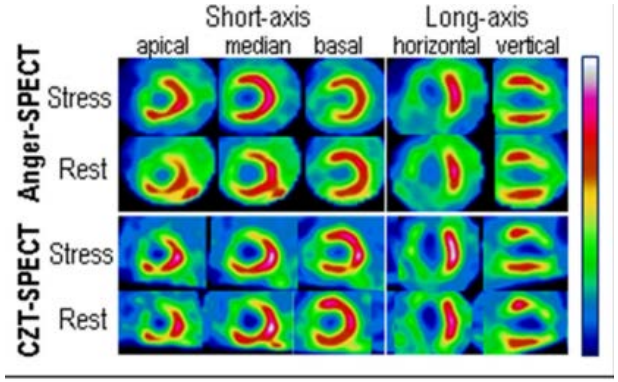
Future development of existing applications

Solid state (CZT) detectors and dedicated camera systems

- Substantially increased sensitivity and spatial resolution of ^{99m}Tc images
- Faster data acquisition, reduced radiation exposure
- Clinical use has started for myocardial perfusion imaging

Improved software for data analysis

- Operator independent reporting
- Quantitative instead of qualitative reporting



Multimodal imaging (SPECT/CT)

- "One stop-shop"

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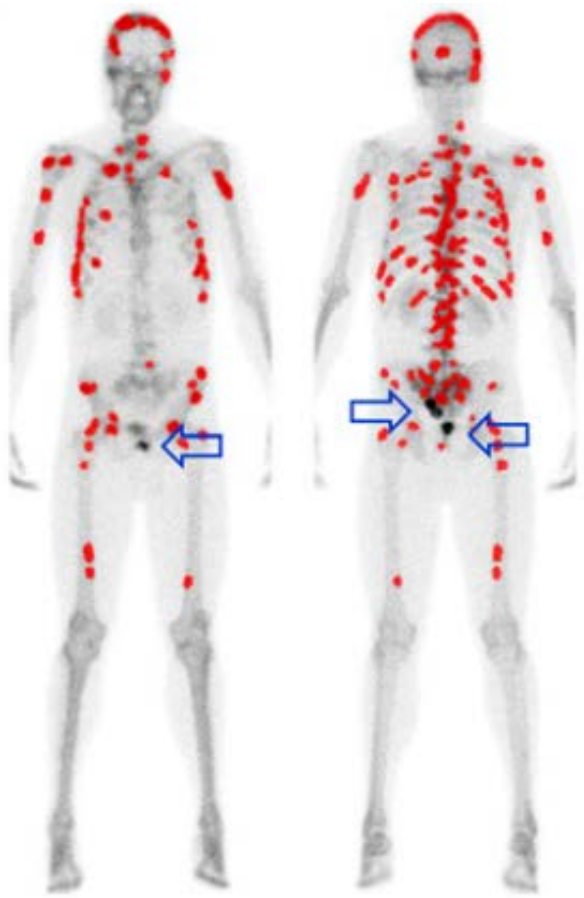
Bone Scan Index (BSI)

- Imbriaco M et al: A new parameter for measuring metastatic bone involvement by prostate cancer: the Bone Scan Index. Clin Cancer Res. 1998 4(7):1765-72.
- Time consuming and complex to calculate manually
- Can now be calculated operator independently by imaging processing software
- Objective definition of disease progression in prostate cancer



Automated measurement of BSI

Anand et al. J Nucl Med (2016) 57:41-45, Figure 3

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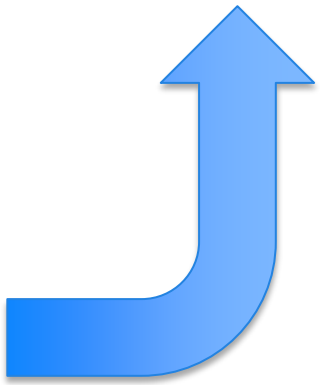
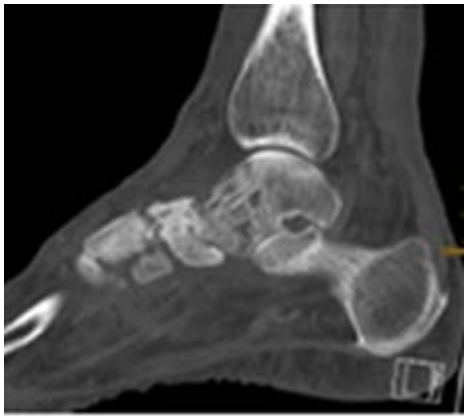
SPECT/CT with ^{99m}Tc-DPD as "one stop shop" to evaluate of bone pain



"Acute arthritis of the talonavicular joint"



"Something is wrong with the bones of the right foot"

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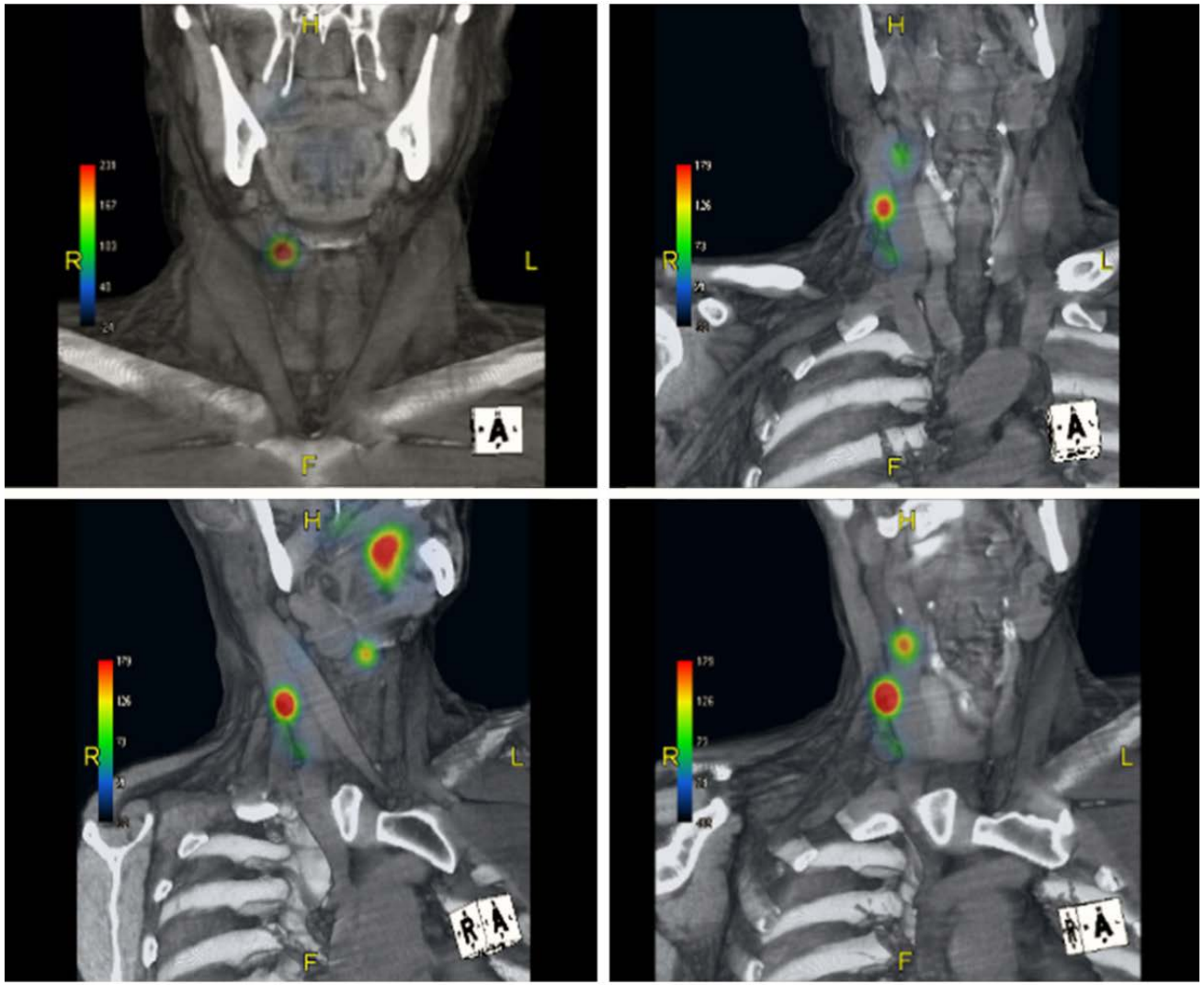
New developments

- Development of new ^{99m}Tc labeled pharmaceuticals has been very slow in the last 20 years
- Focus of research was on PET imaging agents because of the higher sensitivity and easier quantification of PET signals
- Unique advantages of ^{99m}Tc compared to PET radiopharmaceuticals
  - Intraoperative detection/imaging is significantly easier due to lower gamma energy
  - ^{99m}Tc can be used for dual-isotope imaging allowing for multiparametric imaging
  - Longer physical half-life compared to ^{18}F allows for higher image contrast, radiation exposure is lower than for long-lived PET isotopes
- New camera systems (solid state detectors) and sophisticated reconstruction algorithms are decreasing the difference in sensitivity/quantification of gamma camera imaging as compared to PET

Imaging of lymphatic drainage with ^{99m}Tc-Tilmanocept



Agrawal et al. MD Anderson Ann Surg Oncol (2015) 22:3708–3715, Fig 1

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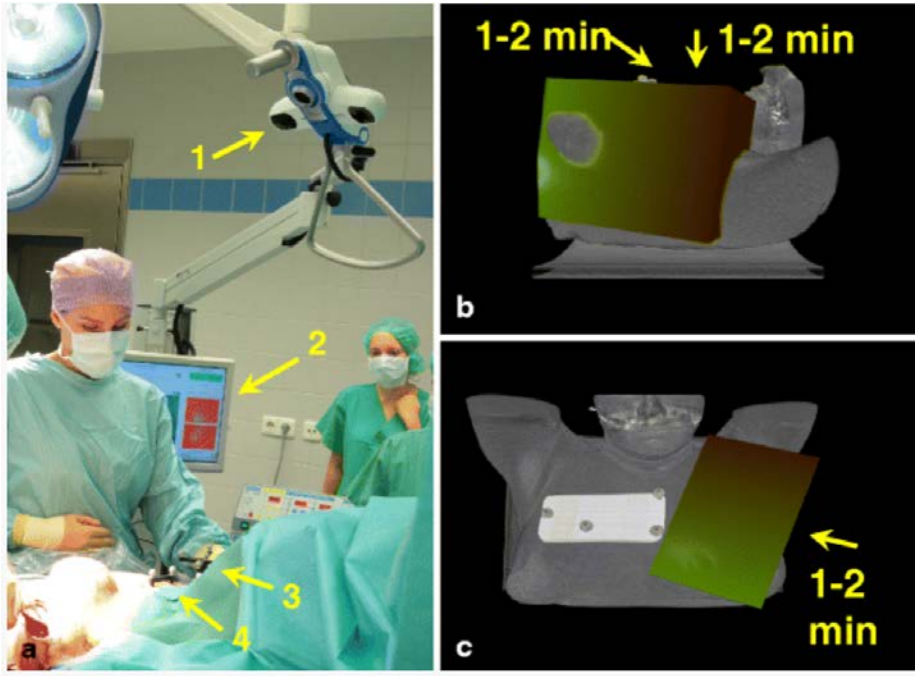
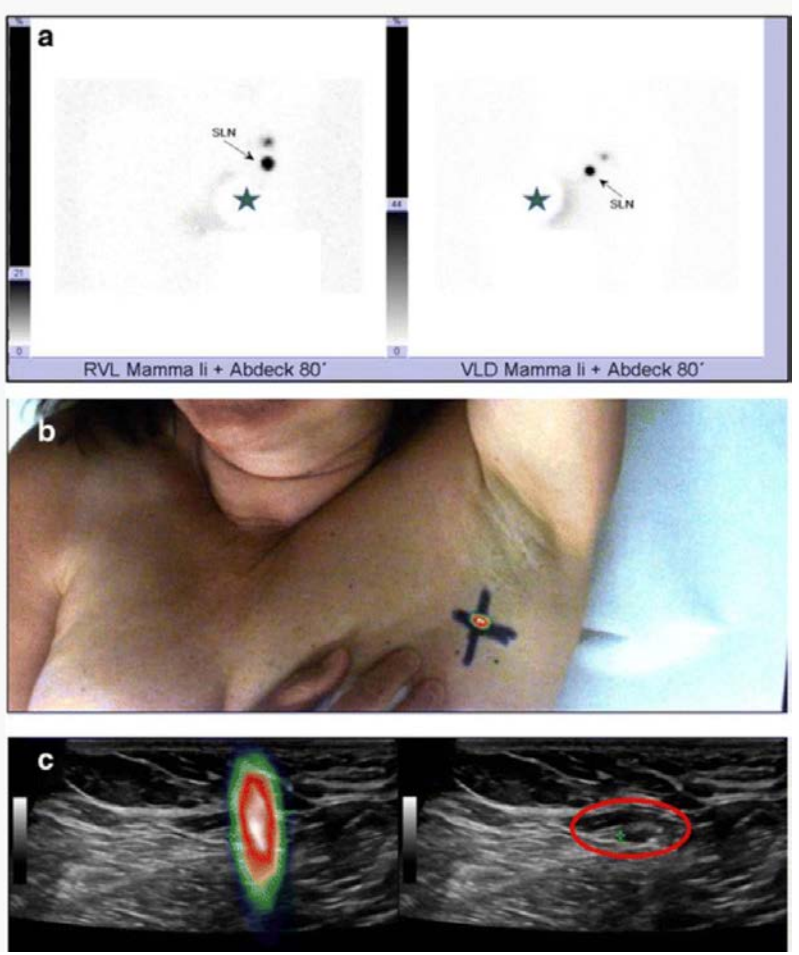
Intraoperative free-hand SPECT and ultrasound fusion





Wendler et al. Technical University Munich Eur J Nucl Med Mol Imaging (2010) 37: 1452, Figure1
Bluemel et al. University of Wuerzburg, Eur J Nucl Med Mol Imaging (2016) 43:2304, Figure 2

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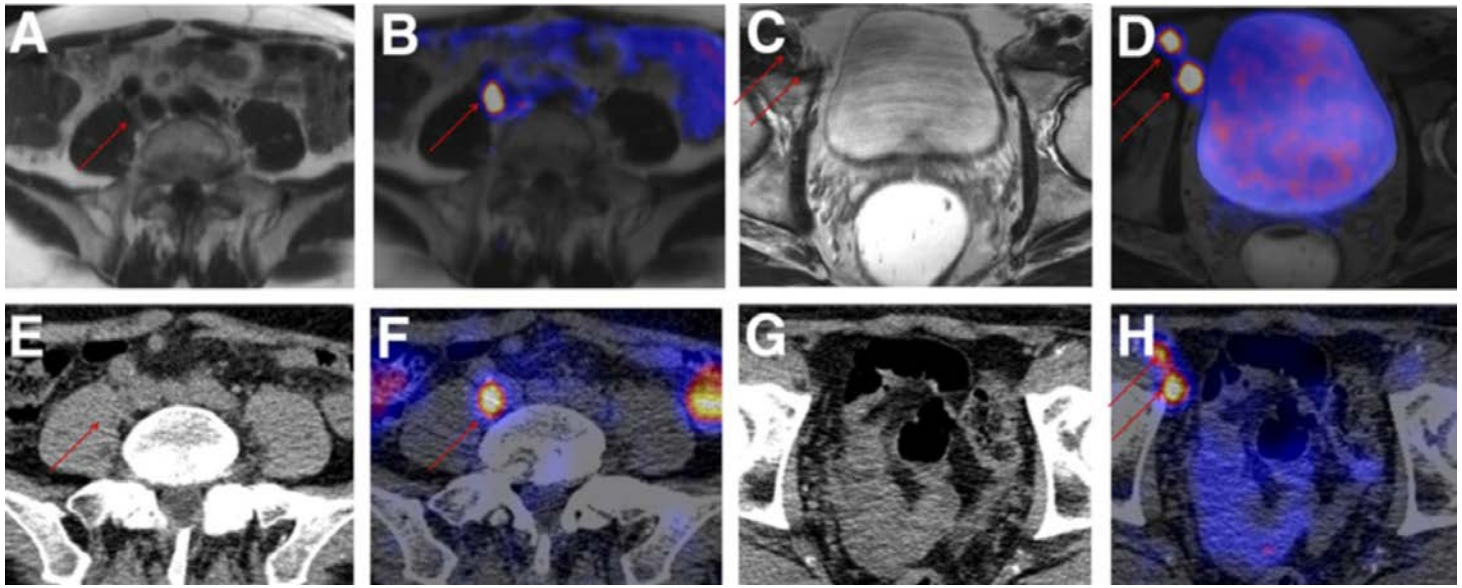
New Imaging agents labeled with ^{99m}Tc

Prostate specific membrane antigen (PSMA) for staging of prostate cancer

PSMA PET/MR

PSMA SPECT/CT



Robu et al. Technical University Munich, J Nucl Med 2017, 58:235-242
Figure 2

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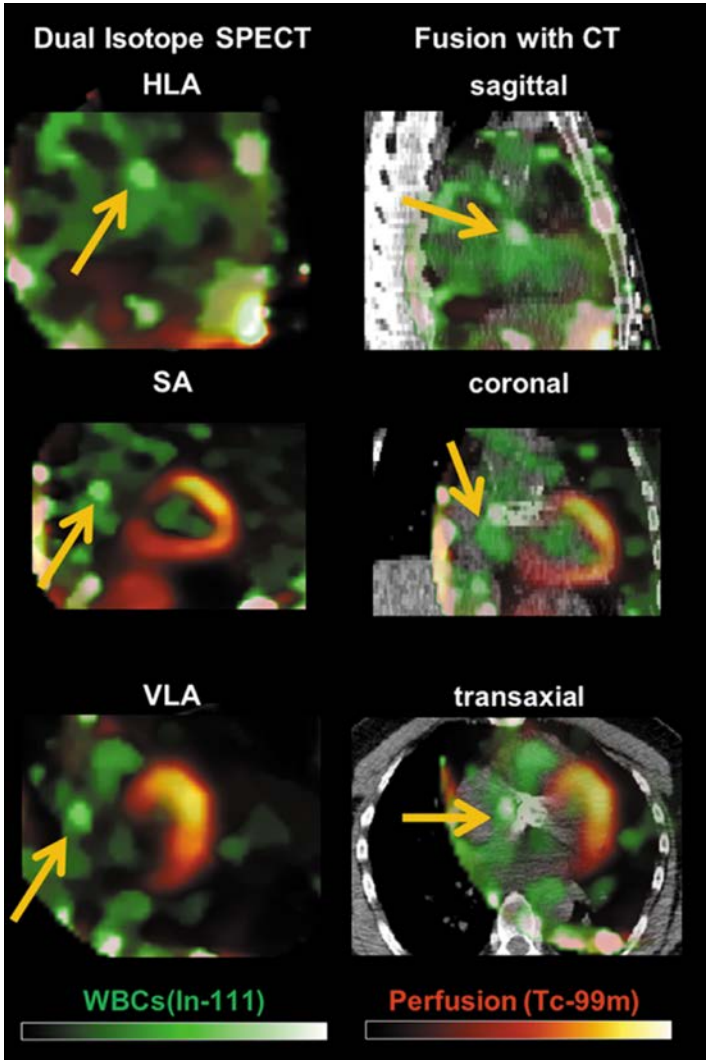
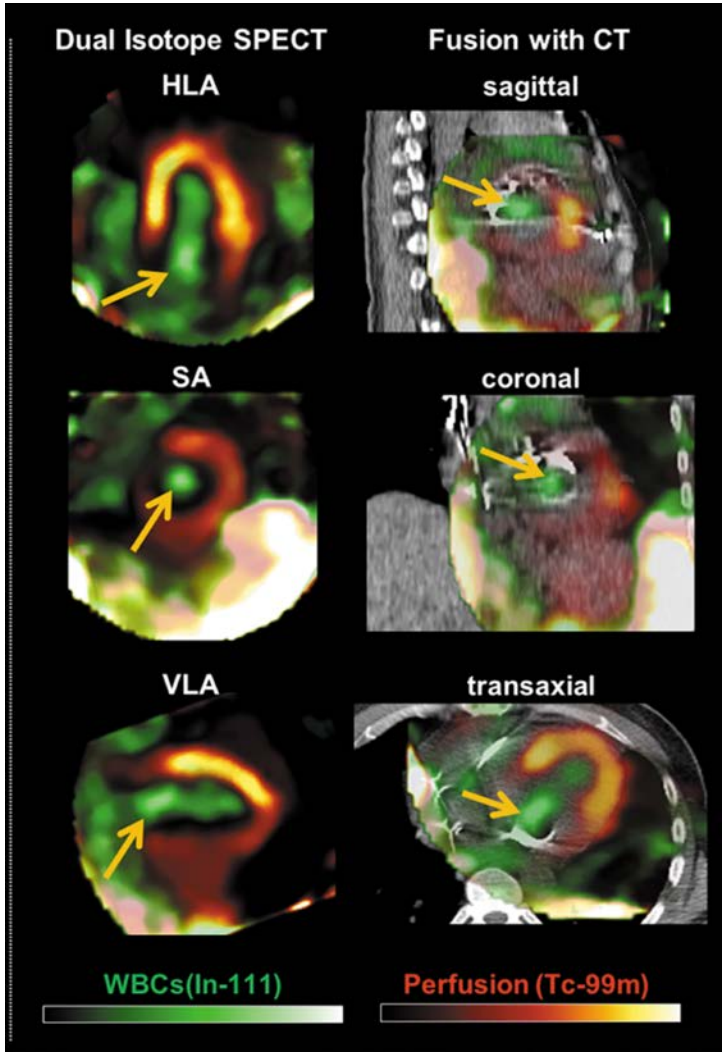
Dual isotope SPECT/CT for detection of endocarditis





Caobelli et al. Eur Heart J 38:436-443, Figure 2,3

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Conclusions

- The medical use of technetium-99m has decreased during the last 10 years due to changes in the reimbursement system and the success of competing imaging modalities (PET/CT, MRI, CT angiography)
- However, there a several indications for which there are no cost-effective alternatives
- New camera systems and new technetium-99m labeled radiopharmaceuticals have the potential to increase the future demand for this radioisotope or at least keep the demand stable