# Mortality in the United States (2006)

<table>
<thead>
<tr>
<th>Rank</th>
<th>Cause of Death</th>
<th>No. of deaths</th>
<th>% of all deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Heart Diseases</td>
<td>631,636</td>
<td>26.0</td>
</tr>
<tr>
<td>2.</td>
<td>Cancer</td>
<td>559,888</td>
<td>23.1</td>
</tr>
<tr>
<td>3.</td>
<td>Cerebrovascular diseases</td>
<td>137,119</td>
<td>5.7</td>
</tr>
<tr>
<td>4.</td>
<td>Chronic lower respiratory diseases</td>
<td>124,583</td>
<td>5.1</td>
</tr>
<tr>
<td>5.</td>
<td>Accidents (unintentional injuries)</td>
<td>121,599</td>
<td>5.0</td>
</tr>
<tr>
<td>6.</td>
<td>Diabetes mellitus</td>
<td>72,449</td>
<td>3.0</td>
</tr>
<tr>
<td>7.</td>
<td>Alzheimer disease</td>
<td>72,432</td>
<td>3.0</td>
</tr>
<tr>
<td>8.</td>
<td>Influenza &amp; pneumonia</td>
<td>56,326</td>
<td>2.3</td>
</tr>
<tr>
<td>9.</td>
<td>Nephritis*</td>
<td>45,344</td>
<td>1.9</td>
</tr>
<tr>
<td>10.</td>
<td>Septicemia</td>
<td>34,234</td>
<td>1.4</td>
</tr>
</tbody>
</table>

*Includes nephrotic syndrome and nephrosis
Source: US Mortality Data 2006, National Center for Health Statistics, CDC, 2009
Change in US Death Rates* from 1991 to 2006

Rate Per 100,000

- Heart diseases
  - 1991: 313.0
  - 2006: 200.2

- Cerebrovascular diseases
  - 1991: 63.3
  - 2006: 43.6

- Influenza & pneumonia
  - 1991: 34.8
  - 2006: 17.8

- Cancer
  - 1991: 215.1
  - 2006: 180.7

* Age-adjusted to 2000 US standard population
Sources: US Mortality Data, National Center for Health Statistics, CDC, 2009
Continuing Evolution of Imaging

Anatomy
- X-Ray
- Computer Tomography (CT)
- Angiography
- Ultrasound /SPECT/ PET
- Magnetic resonance Imaging (MRI)

Contrast-kinetics
- Perfusion
- Metabolism
- Receptors
- Gene Expression
- Signal Transduction
- Cell Trafficking

Biology
- Tracer Technique ($\mu$SPECT,$\mu$PET)
- Optical Imaging

MIPS
Molecular Imaging Program at Stanford

Stanford University
School of Medicine
Department of Radiology
Molecular Imaging

Molecular

Clinic

In vitro

In vivo
Molecular Imaging in Oncology

- Peptide Receptors
- FDG
- Choline
- Antibodies
- Acetate
- Nucleosides
- Enzymes (HSV-Tk)
- Enzymes (Tk)
- O₂
- RGD’s
- PS
- Regional Concentration
- Antisense
- Amino Acids

Stanford University
School of Medicine
Department of Radiology
$^{85}\text{Sr}$ (circa 1966) $^{18}\text{F}$ (circa 1970) $^{87m}\text{Sr}$ (circa 1974) $^{99m}\text{Tc}$ (circa 1974)

$^{99m}$Tc MDP
Dynamic $^{18}$F NaF PET

Diagnostic $^{18}$F NaF PET
DJD  Single metastasis  Multiple metastases
Prospective Evaluation of $^{99m}$Tc MDP Scintigraphy, $^{18}$F NaF PET/CT, and $^{18}$F FDG PET/CT for Detection of Skeletal Metastases

Mol Imaging Biol (2011)

Andrei Iagaru,¹ Erik Mittra,¹ David W. Dick,² Sanjiv Sam Gambhir¹,²,³,⁴

- 52 patients with proven malignancy, referred for evaluation of skeletal metastases
- 37 men and 15 women, 19 - 84 year-old (average: $55.6 \pm 15.9$)
- 19 sarcoma, 18 prostate cancer, 6 breast cancer, 2 colon cancer, 1 bladder cancer, 1 lung cancer, 1 malignant paraganglioma, 1 lymphoma, 1 gastrointestinal stromal tumor, 1 renal cancer and 1 salivary gland cancer
- $^{99m}$Tc MDP bone scintigraphy, $^{18}$F NaF PET/CT and $^{18}$F FDG PET/CT were subsequently performed within 1 month
73-year-old man with metastatic prostate cancer

- $^{99m}$Tc MDP
- $^{18}$F FDG
- $^{18}$F NaF
73-year-old man with metastatic prostate cancer

$^{18}$F FDG PET/CT

$^{18}$F NaF PET/CT
Diagnostic effectiveness:

<table>
<thead>
<tr>
<th></th>
<th>Bone scan</th>
<th>NaF PET/CT</th>
<th>FDG PET/CT</th>
<th>FDG PET/CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>87.5</td>
<td>95.8</td>
<td>66.7</td>
<td>92.9</td>
</tr>
<tr>
<td>95% CI</td>
<td>75.7–93.0</td>
<td>85.2–99.2</td>
<td>54.7–70.1</td>
<td>83.1–97.2</td>
</tr>
<tr>
<td>Specificity</td>
<td>92.9</td>
<td>92.9</td>
<td>96.4</td>
<td>91.7</td>
</tr>
<tr>
<td>95% CI</td>
<td>82.7–97.6</td>
<td>83.8–95.7</td>
<td>86.2–99.4</td>
<td>80.3–96.7</td>
</tr>
<tr>
<td>PPV</td>
<td>91.3</td>
<td>92.0</td>
<td>94.1</td>
<td>92.9</td>
</tr>
<tr>
<td>95% CI</td>
<td>79.0–97.1</td>
<td>81.8–95.2</td>
<td>77.3–98.9</td>
<td>83.1–97.2</td>
</tr>
<tr>
<td>NPV</td>
<td>89.7</td>
<td>96.3</td>
<td>77.1</td>
<td>91.7</td>
</tr>
<tr>
<td>95% CI</td>
<td>79.9–94.2</td>
<td>86.9–99.3</td>
<td>69.0–79.5</td>
<td>80.3–96.7</td>
</tr>
<tr>
<td>Accuracy</td>
<td>90.4</td>
<td>94.2</td>
<td>82.7</td>
<td>92.3</td>
</tr>
<tr>
<td>95% CI</td>
<td>79.5–95.5</td>
<td>84.4–97.3</td>
<td>71.7–85.8</td>
<td>81.8–97.0</td>
</tr>
</tbody>
</table>

CI confidence interval, PPV positive predictive value, NPV negative predictive value
10 participants (5 men, 5 women, 47-81 year-old) diagnosed with cancer and known osseous metastases

- The diagnoses included breast cancer (5 participants), prostate cancer (3 participants), salivary gland cancer (1 participant) and renal cancer (1 participant)

- $^{18}$F NaF PET/CT, $^{18}$F FDG PET/CT and WBMRI were performed within 1 month for each participant
The image quality and evaluation of extent of disease was superior by $^{18}$F NaF PET/CT compared to $^{99m}$Tc-MDP scintigraphy in all patients with skeletal lesions and compared to $^{18}$F FDG PET/CT in 3 of the patients with skeletal metastases.

$^{18}$F NaF PET/CT showed osseous metastases where $^{18}$F FDG PET/CT was negative in another 3 participants.

Extra-skeletal metastases were identified by $^{18}$F FDG PET/CT in 6 participants.

WBMRI with the combination of IDEAL, STIR and DWI pulse sequences showed fewer lesions than $^{18}$F NaF PET/CT in 5 patients, same number of lesions in 2 patients and more lesions in 1 patient.

When compared to $^{18}$F FDG, WBMRI showed fewer lesions in 3 patients and the same amount of lesions in 6 patients.
Combined $^{18}$F-Fluoride and $^{18}$F-FDG PET/CT Scanning for Evaluation of Malignancy: Results of an International Multicenter Trial

Andrei Iagaru¹, Erik Mittra¹, Camila Mosci¹, David W. Dick¹, Mike Sathekge², Vineet Prakash³, Victor Iyer³, Paula Lapa⁴, Jorge Isidoro⁴, Joao M. de Lima⁴, and Sanjiv Sam Gambhir⁵

- 115 patients with proven malignancy who had separate $^{18}$F NaF PET/CT, $^{18}$F FDG PET/CT and a combined $^{18}$F NaF/$^{18}$F FDG PET/CT scans for evaluation of malignancy (total of 3 scans each)
- 63 men and 52 women, 19-84 year-old (average: $58.5 \pm 14.3$)
- Tumor type: prostate cancer (41 participants), breast cancer (39 participants), sarcoma (22 participants), and other cancers (13 participants)
- The interval between the first and third scan ranged 3-28 days (average: $6.7 \pm 4.9$ days)
- A direct comparison for each detected lesion was performed among the 3 scans
74 year-old man with metastatic prostate cancer
### Comparison of PET/CT Scans

<table>
<thead>
<tr>
<th></th>
<th>$^{18}$F FDG PET/CT</th>
<th>$^{18}$F NaF PET/CT</th>
<th>$^{18}$F NaF &amp; $^{18}$F FDG PET/CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skeletal lesions</td>
<td>38/115</td>
<td>67/115</td>
<td>67*/115</td>
</tr>
</tbody>
</table>

- $^{18}$F NaF PET/CT and $^{18}$F FDG PET/CT scans identified malignant lesions in 82/115 enrolled patients (71.3%).
- 19 participants: $^{18}$F NaF > $^{18}$F FDG (osseous metastases)
- 29 patients: $^{18}$F NaF positive, $^{18}$F FDG negative (osseous metastases)
- 18 participants: $^{18}$F NaF = $^{18}$F FDG (osseous metastases)
- 1 patient: $^{18}$F FDG positive, $^{18}$FNaFG negative (osseous metastases)
- 48 participants had no osseous metastases identified on the $^{18}$F NaF PET/CT or the $^{18}$F FDG PET/CT scans

*2 skull lesions missed
## Diagnostic effectiveness:

<table>
<thead>
<tr>
<th></th>
<th>CT only</th>
<th>PET/CT</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>FDG</td>
<td>NaF</td>
<td>NaF/FDG</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td>51.9</td>
<td>51.9</td>
<td>92.6</td>
<td>96.3</td>
</tr>
<tr>
<td>95% CI</td>
<td>31.9-71.3</td>
<td>31.9-71.3</td>
<td>75.7-99.1</td>
<td>81.0-99.9</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>75.0</td>
<td>96.9</td>
<td>90.6</td>
<td>84.4</td>
</tr>
<tr>
<td>95% CI</td>
<td>56.6-88.5</td>
<td>83.8-99.9</td>
<td>75.0-98.0</td>
<td>67.2-94.7</td>
</tr>
<tr>
<td><strong>PPV</strong></td>
<td>63.6</td>
<td>93.3</td>
<td>89.3</td>
<td>83.9</td>
</tr>
<tr>
<td>95% CI</td>
<td>40.7-82.8</td>
<td>68.1-99.8</td>
<td>71.8-97.7</td>
<td>66.3-94.5</td>
</tr>
<tr>
<td><strong>NPV</strong></td>
<td>64.9</td>
<td>70.5</td>
<td>93.5</td>
<td>96.4</td>
</tr>
<tr>
<td>95% CI</td>
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</tr>
</tbody>
</table>
33 Prostate Cancer Patients

- In 3 patients the skeletal disease was more extensive on $^{18}$F NaF PET/CT and the combined scan than on $^{18}$F FDG PET/CT

- In 16 patients $^{18}$F NaF PET/CT and the combined scan showed osseous metastases and $^{18}$F FDG PET/CT was negative

- 14 patients had no osseous metastases

- $^{18}$F FDG PET/CT and the combined scan showed extra-skeletal metastases in 5 patients
Gastrin-releasing peptide receptors (GRPr) are highly over-expressed in many human cancers, including prostate cancer

BAY 86-7548 is a bombesin antagonist with high GRPr affinity

5 healthy men were imaged

BAY 86-7548 is safe and had a dosimetry profile similar to other FDA-approved radiopharmaceuticals
$^{18}$F or $^{64}$Cu Bombesin Analogues (at Stanford)

$^{64}$Cu-NODAGA-RM1

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MIPS
Molecular Imaging Program at Stanford

Stanford University
School of Medicine
Department of Radiology
Biodistribution, Tumor Detection, and Radiation Dosimetry of $^{18}$F-DCFBC, a Low-Molecular-Weight Inhibitor of Prostate-Specific Membrane Antigen, in Patients with Metastatic Prostate Cancer


Steve Y. Cho$^{1,2}$, Kenneth L. Gage$^1$, Ronnie C. Mease$^{1,2}$, Srinivasan Senthamizhchelvan$^1$, Daniel P. Holt$^1$, Akimosa Jeffrey-Kwansai$^1$, Christopher J. Endres$^1$, Robert F. Dannals$^1$, George Sgouros$^1$, Martin Lodge$^1$, Mario A. Eisenberger$^2$, Ronald Rodriquez$^{2,3}$, Michael A. Carducci$^3$, Camilo Rojas$^4$, Barbara S. Slusher$^4$, Alan P. Kozikowski$^5$, and Martin G. Pomper$^{1,2}$

- 5 patients with radiologic evidence of metastatic prostate had 10 mCi of $^{18}$F DCFBC
- 32 PET-positive suspected metastatic sites were identified, with 21 concordant on both PET and conventional imaging for abnormal findings compatible with metastatic disease
- Of the 11 PET-positive sites not identified on conventional imaging, most were within the bone and could be considered suggestive for the detection of early bone metastases
PET imaging with a $[^{68}\text{Ga}]$gallium-labelled PSMA ligand for the diagnosis of prostate cancer: biodistribution in humans and first evaluation of tumour lesions

37 patients with prostate cancer and rising PSA levels had $^{68}\text{Ga}$-PSMA PET/CT

31 patients (83.8 %) showed at least one lesion suspicious for cancer at a detection rate of 60% at PSA <2.2 ng/ml and 100% at PSA >2.2 ng/ml

Median tumour to background ratios were 18.8 (2.4-158.3) in early images and 28.3 (2.9-224.0) in late images
82 consecutive patients with biochemical relapse after radical prostatectomy

18F Choline PET/CT detected recurrent lesions in 51 of the 82 patients (62%)

The median PSA value was significantly higher in PET-positive than in PET-negative patients (4.3 ng/ml vs. 1.0 ng/ml; \( P < 0.01 \))

The optimal PSA threshold from ROC analysis for the detection of recurrent prostate cancer lesions was 1.74 ng/ml (AUC 0.818, 82% sensitivity, 74% specificity)

PSA doubling time suggested a threshold of 3.2 months, but this failed to reach statistical significance (\( P = 0.071 \))
(S)-4-(3-18F-Fluoropropyl)-l-Glutamic Acid: An 18F-Labeled Tumor-Specific Probe for PET/CT Imaging—Dosimetry


Kamilla Smolarz¹, Bernd Joachim Krause¹, Frank-Philipp Graner¹, Franziska Martina Wagner¹, Christina Hultsch², Claudia Bacher-Stier², Richard B. Sparks³, Susan Ramsay³, Lüder M. Fels², Ludger M. Dinkelborg²,⁴, and Markus Schwaiger⁴

- 18F FSPG is a glutamic acid derivative
- Already studied in HCC, breast and lung cancers in South Korea
- 10 prostate cancer, 5 H&N cancer, 5 colorectal cancer, 5 NHL and 5 brain cancer patients were imaged at Stanford
- 18F FSPG is safe and has a dosimetry profile similar to other FDA-approved radiopharmaceuticals
Metabolic pathways and the role of $^{18}$F FSPG
"Advocates of evidence based medicine have criticized the adoption of interventions evaluated by using only observational data.

We think that everyone might benefit if the most radical protagonists of evidence based medicine organized and participated in a double blind, randomized, placebo controlled, crossover trial of the parachute.

Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomized controlled trials.

THANK YOU!

http://nuclearmedicine.stanford.edu

http://mips.stanford.edu