Faculty of Health Sciences

PET/CT and PET/MRI

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Clinical Physiology, Nuclear Medicine & PET
Rigshospitalet, University of Copenhagen & Technical University of Denmark

November, 13th 2023 DTU

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Rigshospitalet

- University hospital
- 12.000 staff, 250 ph.d.s, 3500 publications, 120 professorer
- Founded in 1757 as the first hospital in the Nordic countries to cure patients and do research

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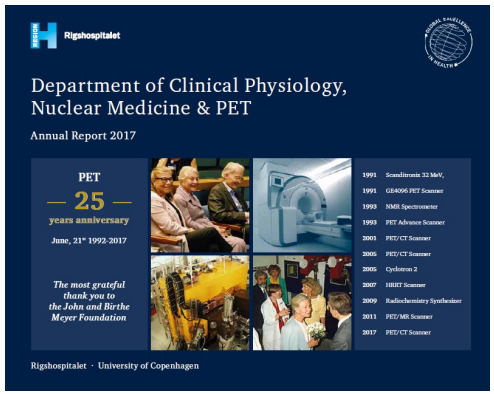

130.000 studies/year, 160 publikations, 200 staf, 25 Ph.d., 6 professors,

2 cyklotrons, 7 PET/CT, PET/MRI, micro-PET and MRI, ½ bio. dk.kr.

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Liselotte Højgaard (1957), MD 1982, specialist clinical physiology & nuclear medicine.

Chair of Dept. of Clinical Physiology, Nuclear medicine & PET, 2000-2023 Rigshospitalet. Prof. University of Copenhagen and DTU.

Chair of The Danish National Research Foundation 2013-2018.

Editor, Ugeskrift for Læger 1996-2002. ICMJE, The Vancouver Group.

Chair EMRC, ESF 2006-2012. Chair EU AG Health research 2010-2017.

Board member the Novo Nordisk Foundation, Die Robert Bosch Stiftung, Stuttgart, ERC Scientific Council.

The Royal Danish Academy of Sciences and Letters & ATV The Academy of Technical Sciences.

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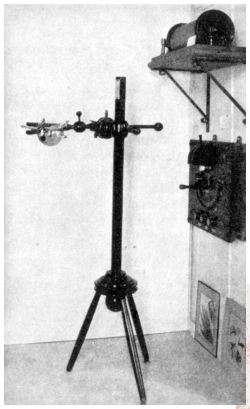

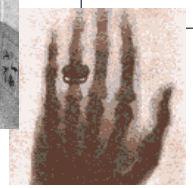

X-rays were described for the first time by Wilhelm Conrad Röntgen, Würzburg, in 1895.

1044 papers about X-rays in medicine were published in 1896.

The first X-ray machine Copenhagen 1896

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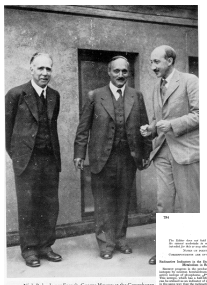
Nuclear Medicine was born in Copenhagen



Niels Bohr, James Franck, George Hevesy at the Copenhagen
Courtesy: The Niels Bohr Archive.

Nuclear Medicine was developed in Copenhagen by Georg de Hevesy & Niels Bohr and published in 1935.

Hevesy won the Nobel Prize in 1943 for the tracer technique.

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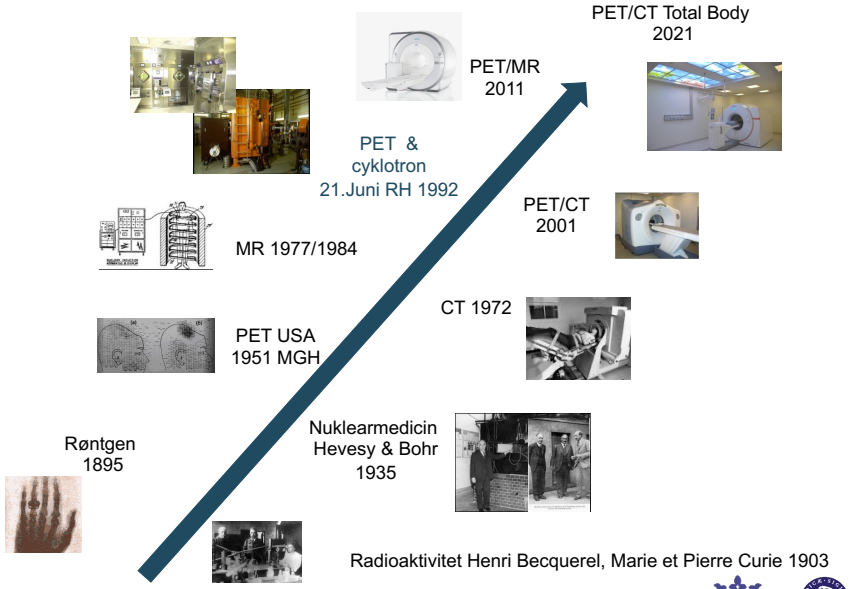

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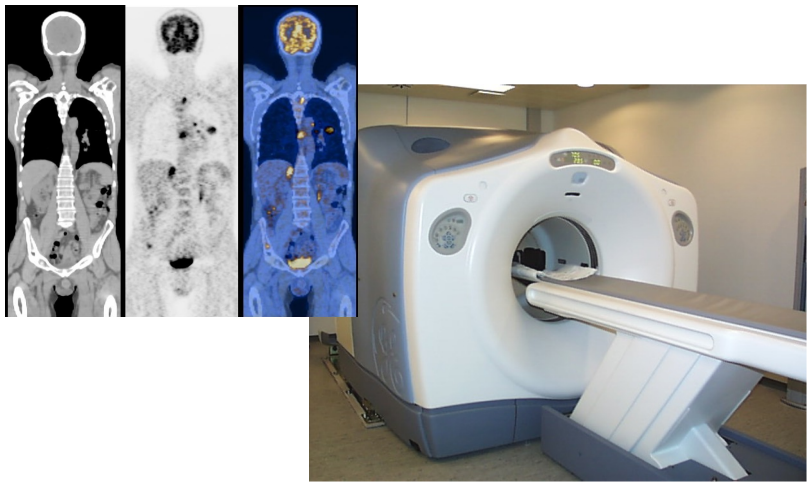

PET/CT December 2001

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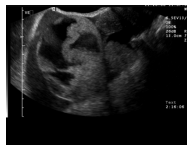
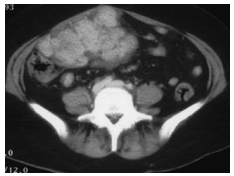
Diagnostic imaging in cancer

Diagnosis
Staging – how widespread is the disease ?
Treatment effect
Relapse – has the disease reappeared
Planning of surgery and radiation therapy



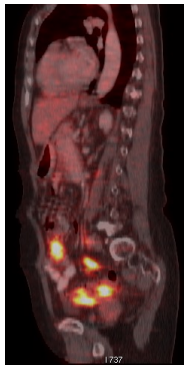
Ultrasound



CT

MR

PET/CT

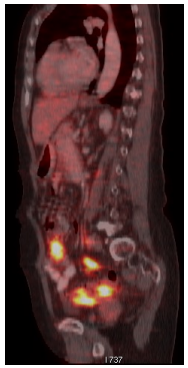


CT and MRI have key roles for the diagnosis of orbital tumors

Many diseases, many methods, which one ?

PET/CT

Diagnostic accuracy – sensitivity and specificity
Prize
Side effects
Availability
Cost effectiveness
> 10.000 articles



Ultrasound **CT** **MR**

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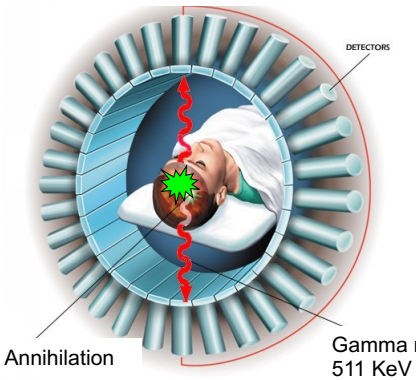
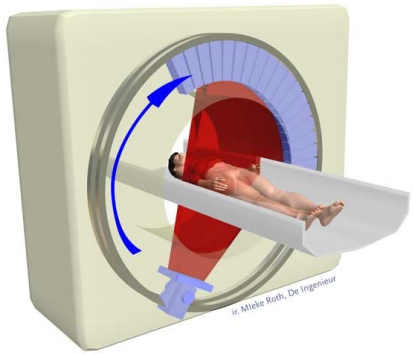
PET positron emission tomography

CT computer tomography





F-18 FDG: fluoro-deoxyglucose is a glucose analogue, showing glucose metabolisme.
Cancer cells have a high glucose metabolism; F-18 decays via positrons.

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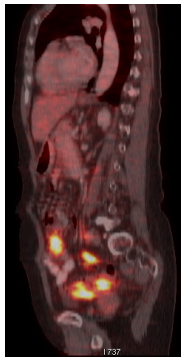
PET/CT-indications 2023



Dementia, brain tumors, Parkinson's disease

Heart - flow and metabolisme

Oncology: staging, treatment effect, relapse, control, RTP- and OP-planning

35.000 publications on PET

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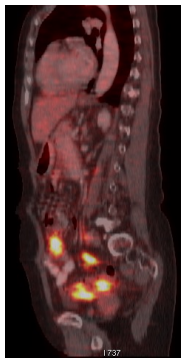
PET/CT as first line imaging



PET/CT with FDG is integrated in Danish routine patient work up "Kræftpakkerne"

- Brain tumors
- Lung cancer
- Cervical and ovarian cancer
- Lymphoma
- Head & Neck
- Gastro-intertinal
- Sarcomas
- Malignant melanoma

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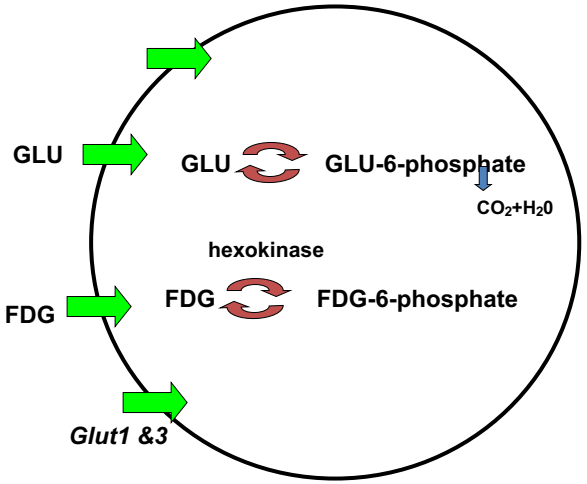
Normal cells use glucose



FDG fluoro-deoxy-glucose

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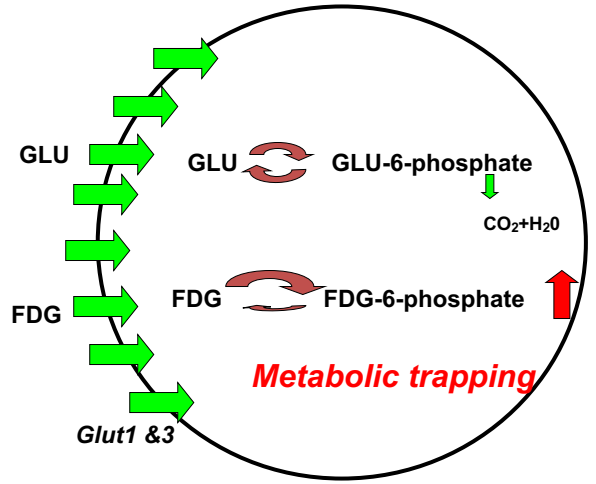
Cancer cells use a lot of glucose



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Radioisotope	Half-life (min)
^{18}F	109.8
^{11}C	20.4
^{13}N	9.96
^{15}O	2.05

FDG: F-18 flouro-deoxy-glucose

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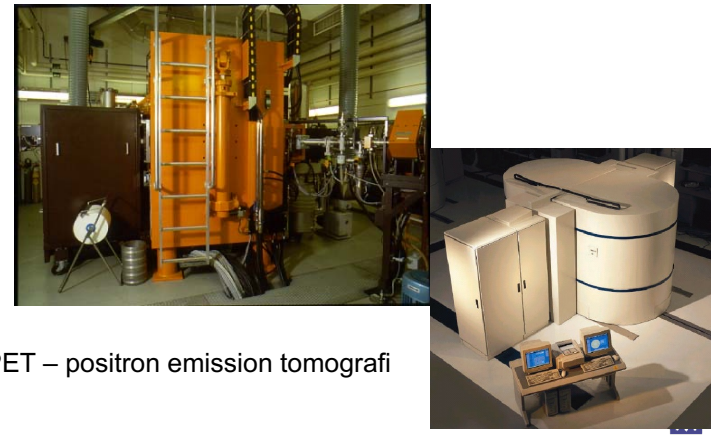
Cyklotrons for isotope production



PET – positron emission tomografi

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Radiochemistry Unit with lead hot cells

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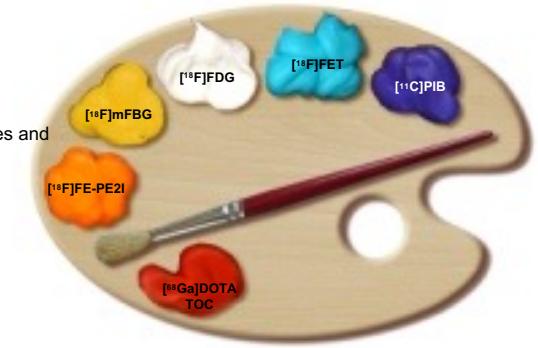
Tracers for PET

Tracers with different biology

For the diagnosis of different diseases and Functional imaging



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PET tracers	Use
[F-18] FDG	Onkology
[F-18] Altanserin	5-HT2A receptors
[C-11] CUMI-101	5-HT1A receptors
[C-11] DASB	Serotonin transporter
[C-11] Flumazenil	Central benzodiazepin receptor
[C-11] PIB	beta-amyloid plaques
[C-11] SB207145	5-HT4 receptors
[O-15] H2O	Brain CBF
[N-13] NH3	Heart flow
[F-18] FLT	Cell proliferation
[Cu-64] ATSM	Hypoxia
[Ga-68] DOTATOC	Somatostatin receptors
[Ga-68] ABY-025	Affibody/HER2 ekspression
[F-18] FET	Brain tumors

Cyklotrons – small 2-3 MeV deuteron-machines ^{15}O-vand

230 - 400 MeV superconducting magnets for particle-therapy

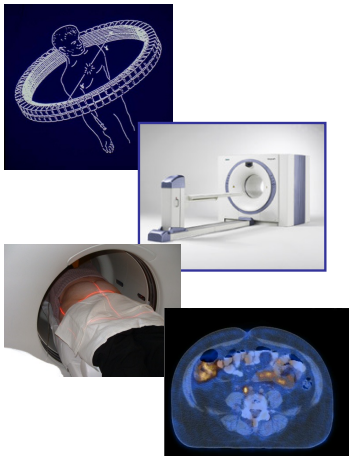
And research in high energy physics (CERN, RIKEN, iThemba).

^{18}F, ^{11}C, ^{13}N og ^{15}O og ^{64}Cu, ^{89}Zr, ^{124}I. Isotopes for PET-tracers

- Increasing demand
- Different tracers
- Focus on security, GMP, supply chain stability, flexibility, research
- Alfa-therapy for theranostics: ligand with **Astatin-211 for treatment, Actinium-225 for diagnosis with PET scan**

Tak til Holger Jensen

”PET - The fastest growing medical technology ever ”



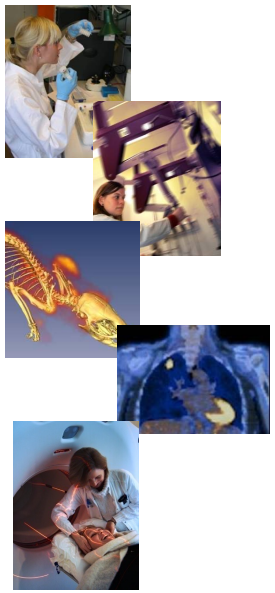
Positron tracer F-18 FDG

Patient injection

PET scanning combined with CT

Interpretation by NM & radiologist

High sensitity and specificity, and game changer for 30 % !



PET research

Basic research – cyclotron isotopes, radiochemistry tracers, scanner hardware and new math algorithms

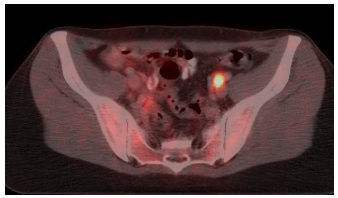
Translational – from lab to clinical patients in animal and man

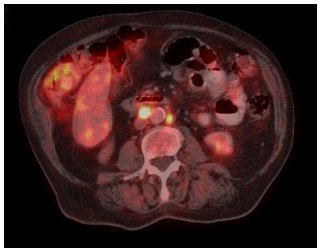
Clinical research – diagnosis, treatment evaluation, relapse, radiation therapy planning

New isotopes, new tracers, new hardware & software, physiology, patophysiology, new drugs, new methods

- non commercial
- private-public partnership
- industry driven

PET/CT in cervical cancer

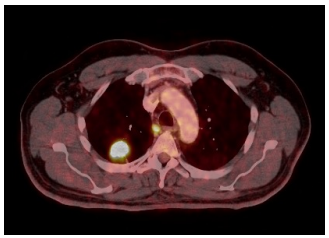




Metastatic lymph nodes:

- **Pelvis**
- **Para-aortal**
- Inguinal
- Mediastinum
- Neck
- Omentum

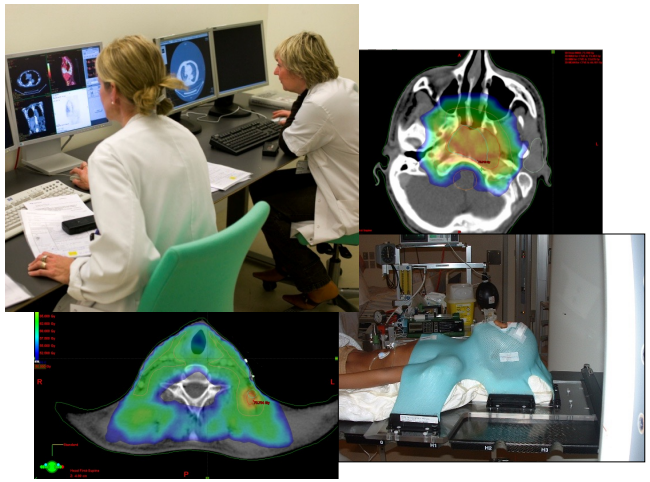
PET/CT and lung cancer



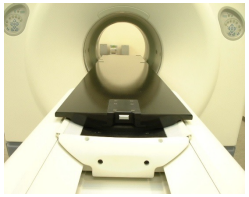
Preoperative staging of lung cancer with combined PET/CT.
Randomized study on PET/CT and lung cancer staging. N= 189, Conventional or same + PET/CT.

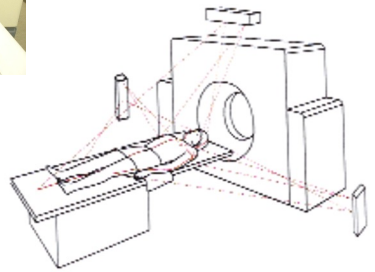
Relative risk reduction for a futile thoracotomy 51 %.

Fischer & Højgaard, New Engl J Med 2009;2,361:92-9



External LAP laser system





PET/CT for planning of radiation therapy

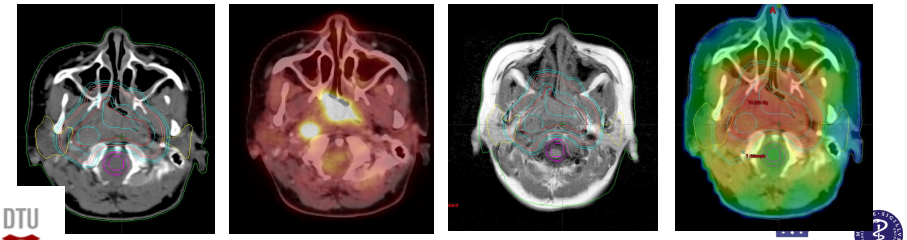
Radiotherapy and imaging

Radiotherapy planned by CT

If tumor is drawn too small possibilities for cure smaller

If tumor is drawn to large side-effects worse

PET and MRI to improve methodology



FDG-PET MRI Treatmentplan

Advance PET scanner 1995

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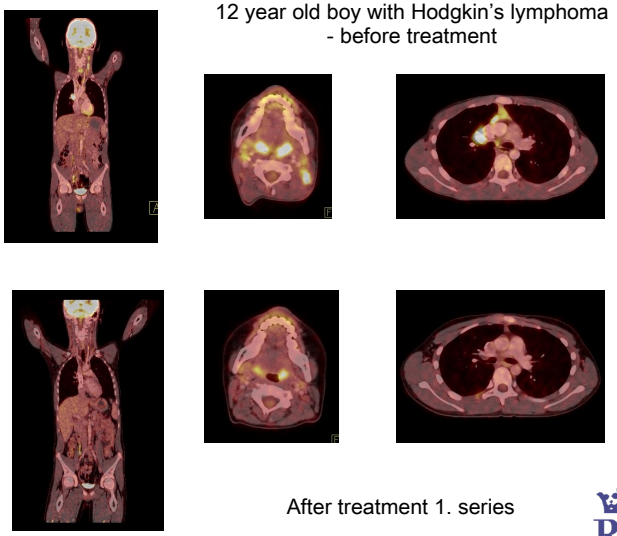
12 year old boy with Hodgkin's lymphoma
- before treatment



After treatment 1. series

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Børneriget – hospital for sick children

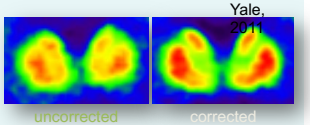
Movement correction for brain MRI

World's first

- Structured light surface scanner with invisible light
- Markerless tracking for MR & PET motion correction

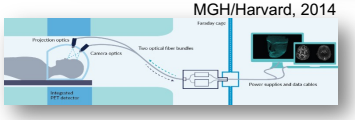
DTU/RH, 2010

Yale, 2011

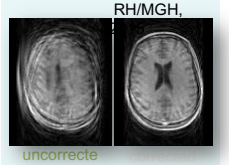


uncorrected corrected

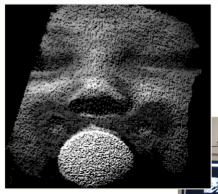
MGH/Harvard, 2014



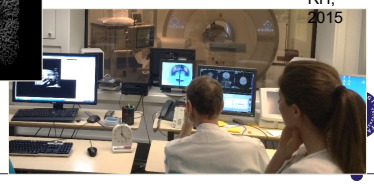
RH/MGH,



uncorrected corrected



RH, 2015



Oline Vinter Olesen
PhD, MSc (Eng. Medicine and Technology)
Founder & CTO, TracInnovations
Senior Researcher, DTU Compute & RH

Cluster for molecular imaging

Development of new tracers .

Early evaluation of new drugs for cancer treatment with molecular imaging using animal studies with PET/CT and PET/MR.

Translational from use in animal to man.

DTU

The Danish National Advanced Technology Foundation

RH

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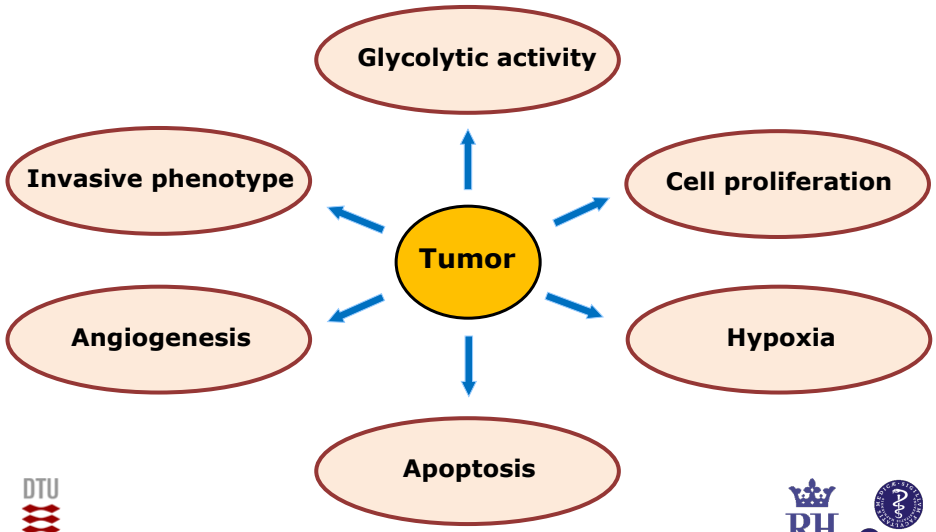
Tissue characteristics



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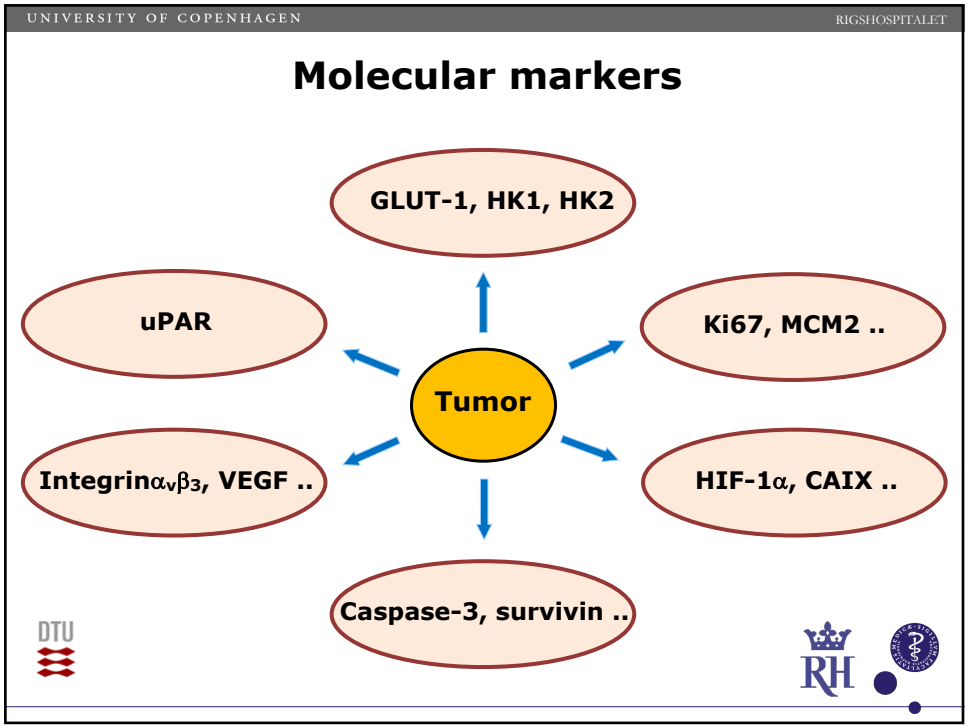
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Molecular markers
GLUT-1, HK1, HK2
uPAR
Ki67, MCM2 ..
Tumor
Integrinαvβ3, VEGF ..
HIF-1α, CAIX ..
Caspase-3, survivin ..
DTU
RH

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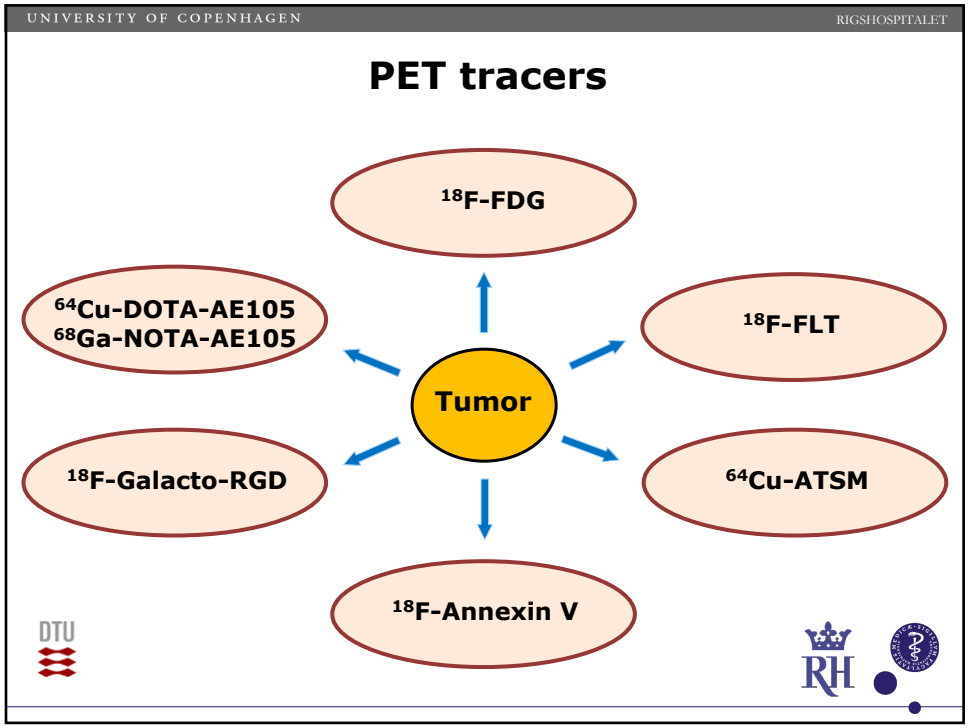
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PET tracers
18F-FDG
64Cu-DOTA-AE105
68Ga-NOTA-AE105
18F-FLT
Tumor
18F-Galacto-RGD
64Cu-ATSM
18F-Annexin V
DTU
RH

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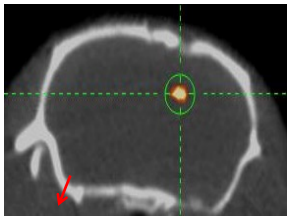
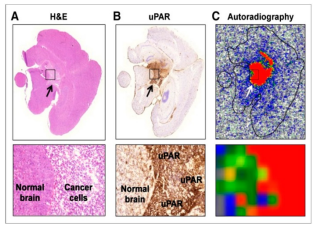
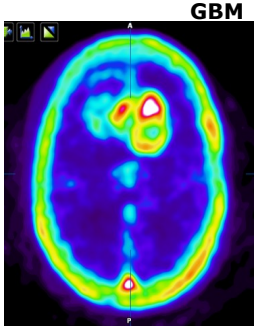
uPAR-PET/MRI of brain cancer – from mouse to man

PDOX GBM





GBM



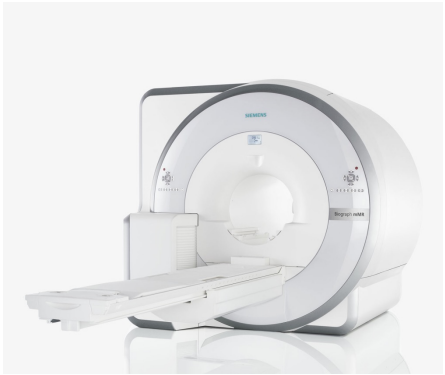
Ex vivo target validation

Prof. Andreas Kjaer et al.

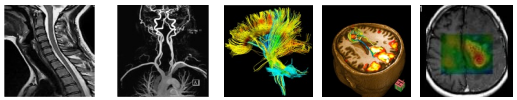
Biograph mMR – the worlds first simultaneous, whole-body molecular MR

Copenhagen PET/MRI

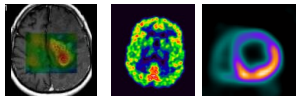
- Simultaneous PET and MRI
- From December 2011



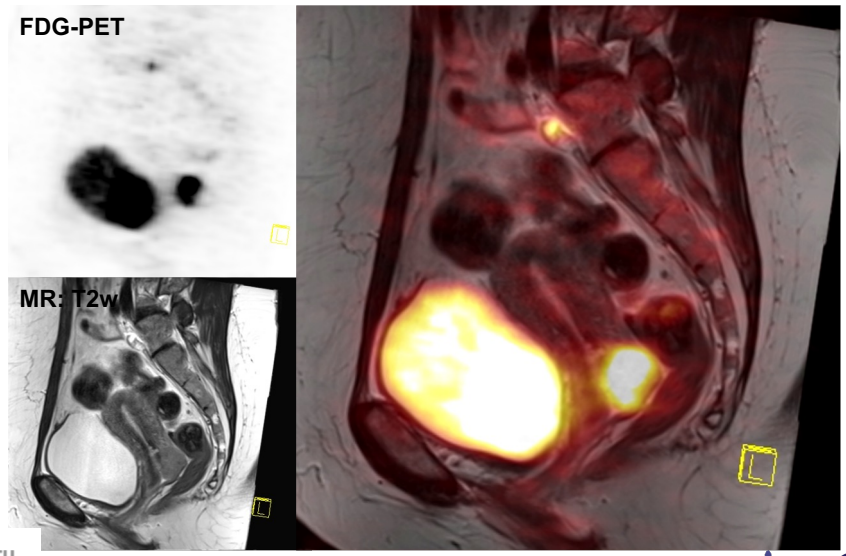
Morphology, physiology & molecular imaging
…….in the same scanner …at the same time



MR



PET



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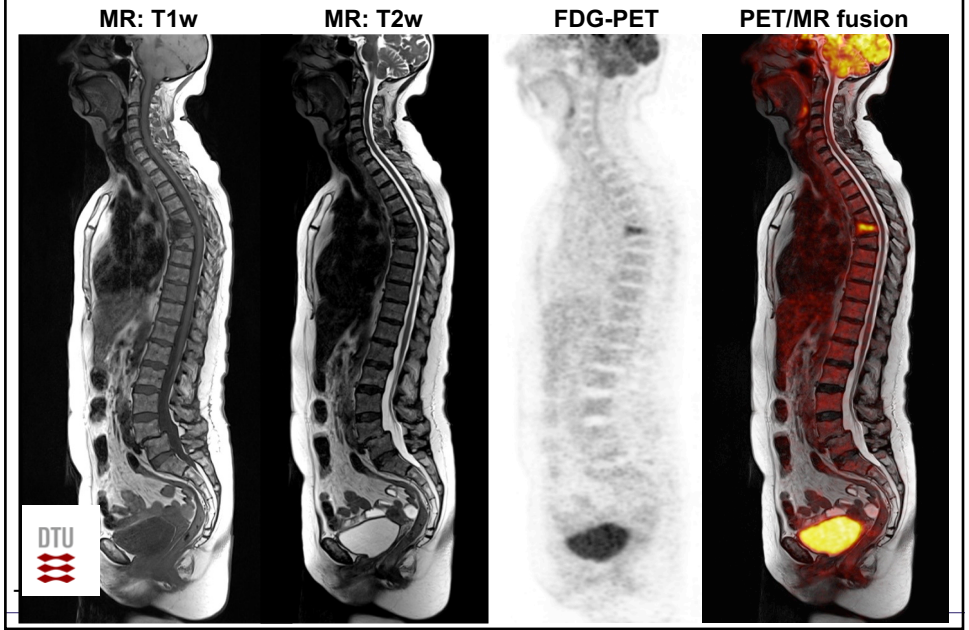
PET funktion og MR anatomi i columna



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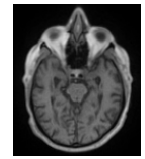
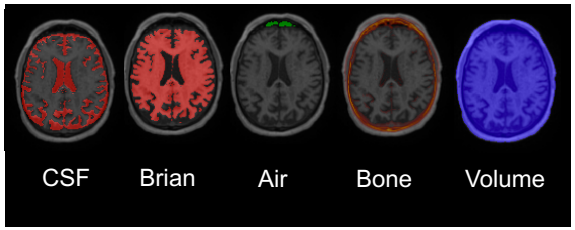
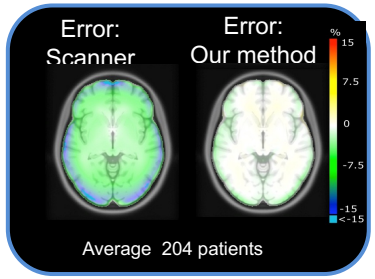
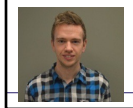
New optimization of PET/MR: RESOLUTE







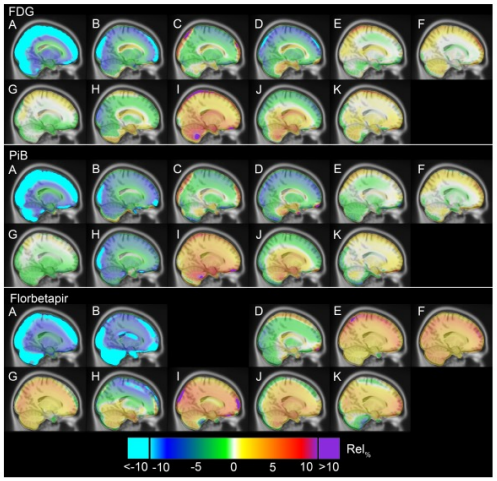
New technique for PET/MR adjusts the reconstruction error. Also useable in children. Error now <1 % on PET-signal



Claes Ladefoged, cand.scient., ph.d.-studerende

46

Multi-center evaluation of 11 PET/MR-correction methods



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AI for better imaging

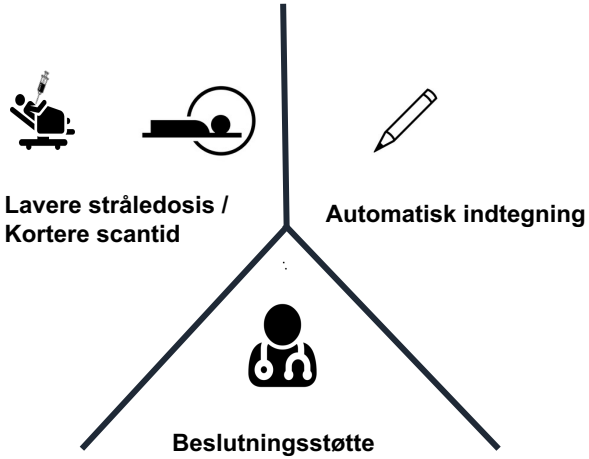
- Better signal to noise ration
- Shorter scan time and reduced dose
- Synthetic data – PET from MRI
- Decision support in MS and dementia
- Analysis and automatic reading ???

DTU

RH

49

CAAI



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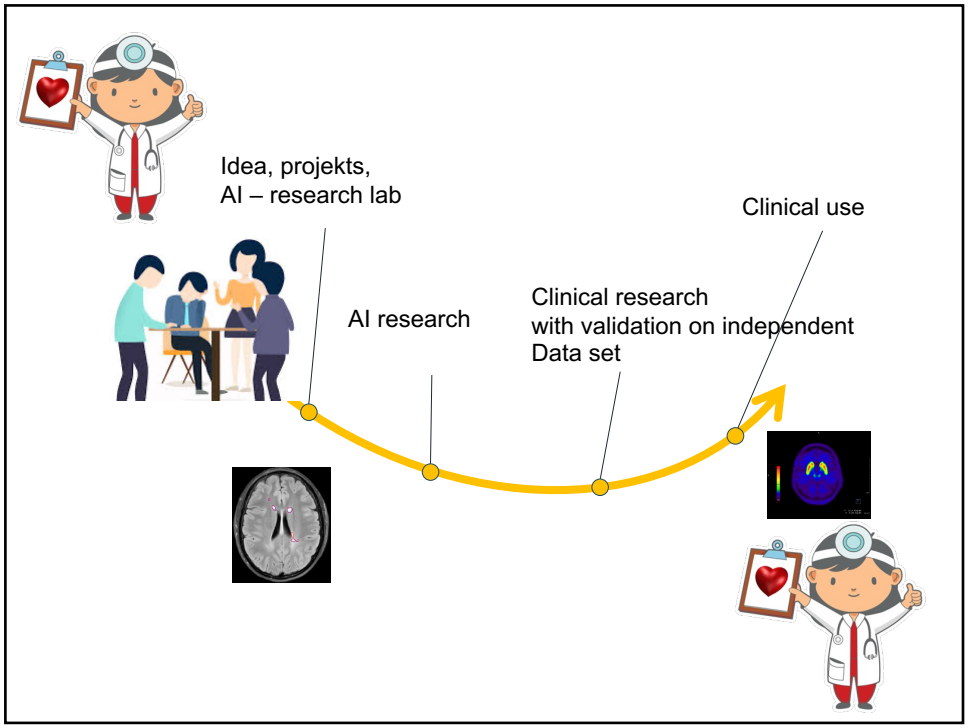
50



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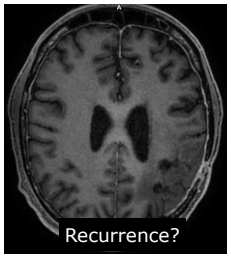
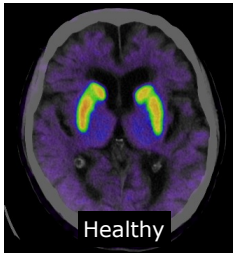
Clinical practice brain studies

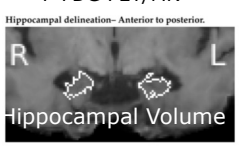
T1 MRI

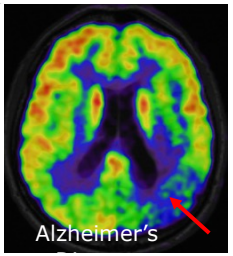


^{18}F-FE-PE2I DaT PET

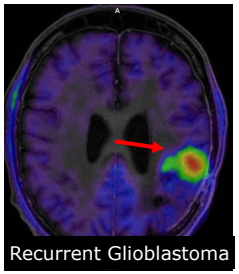


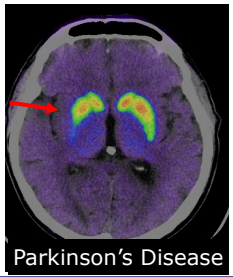
^{18}F-FDG PET/MR





^{18}F-FET PET





Prof. Ian Law

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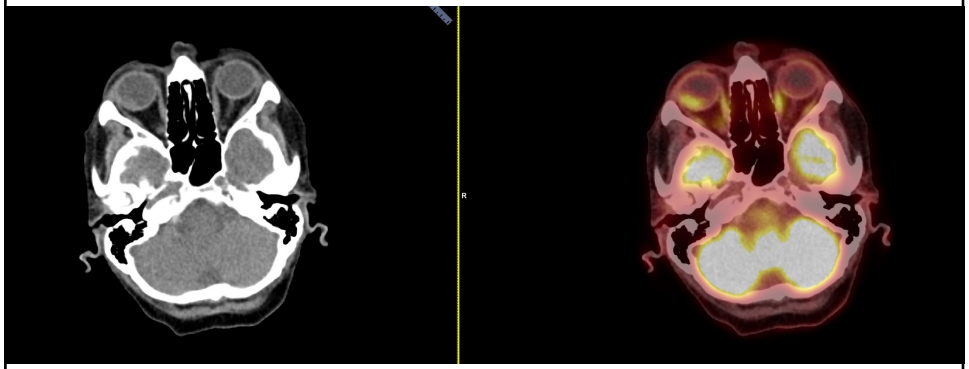
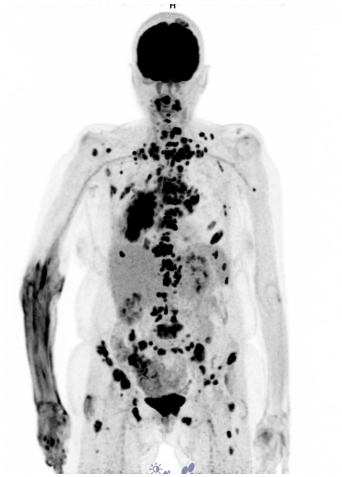


PET/CT revealed a tumour in the right eye

53



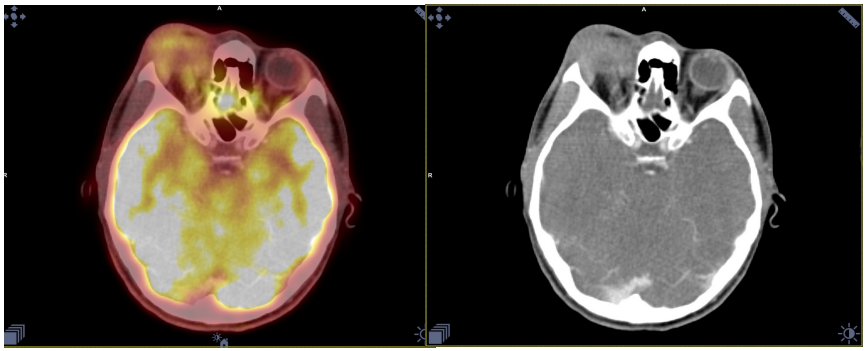
…and several metastases besides a primary tumour in the right lung. Confirmed by biopsy.

54

12 year old boy, previously well, swelling of the right eye. MRI local hospital: proces in right orbita around bulbus.

Normal vision. Biopsy: embryonal rhabdomyosarkoma. WB FDG PET/CT for staging.

55

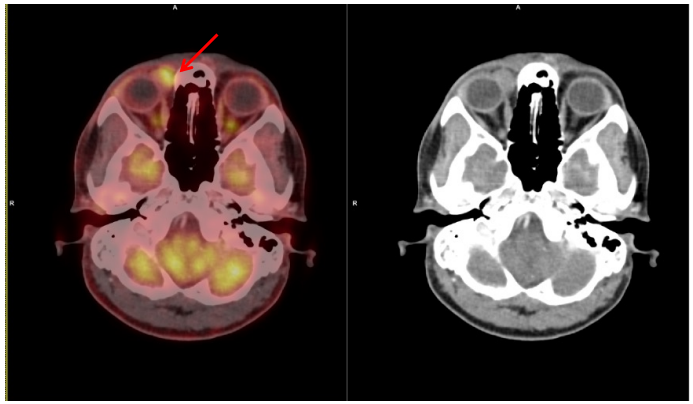


PET/CT : Malignant looking proces in right orbita, extra ocular, no bone involvement and no dissemination.

Chemo- og proton therapy in Houston.

56

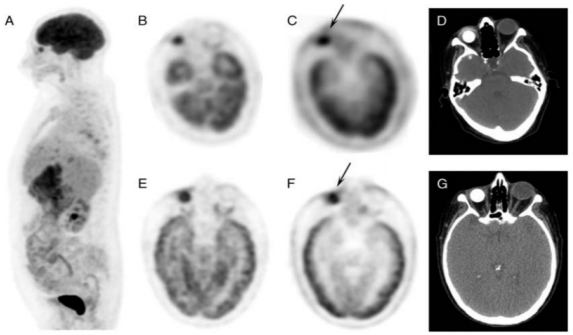
1 year later suspicion of relapse of the rhabdomyosarcoma in the right orbita at control MRI. Referred to WB FDG PET/CT for metabolism in tumor and dissemination ?



Malignant tumor medially in right orbita without signs of dissemination. Chemoterapy, VIT.

57

5
8



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PET/MR and PET/CT and genes and epigenetics and clinical and life style information: ”Personalised medicine”

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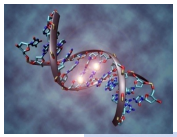
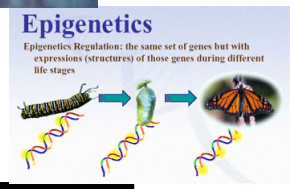
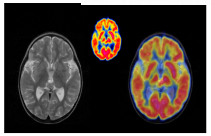
Personalised Medicine







Paradigm shift with tailored prevention, early diagnosis, treatment based on genes and epigenetics &
The deep phenotype with imaging.

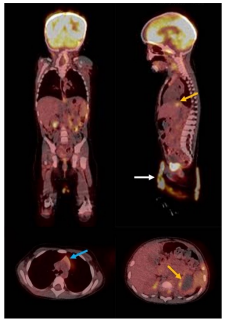
60

"If this does not help, please come again, and we find something else"

"Couldn't I get the something else right away ?"

61

QUADRA Total body PET/CT



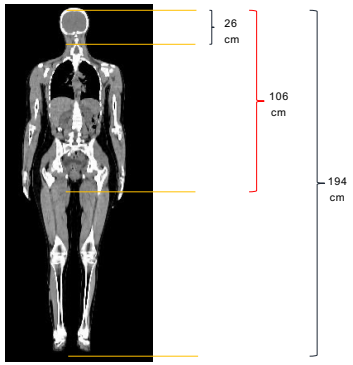
62

Fast scans with high quality and low dose – children no sedation.

Long field-of view to physiologi & patophysiologi with kinetics from dynamic acqusitions - total body system-physiologi.

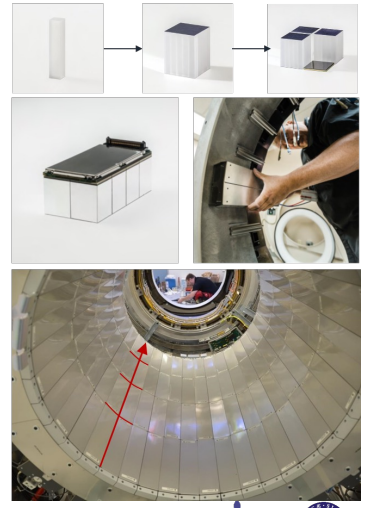
Deep inspiration breath hold for planning of radiotherapy.

63



Sensitivity:
x 10 standard digital scanner
x 40 analog scanner

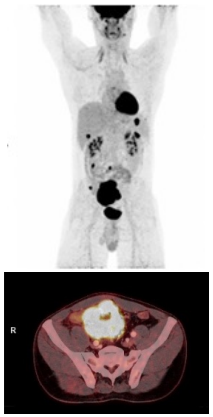
3.2-mm krystal Vision teknologi

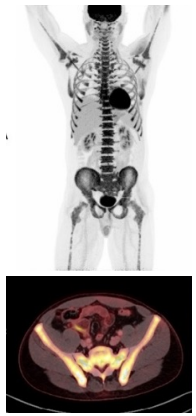


64

Hodgkin lymfoma, before treatment

After 3 series





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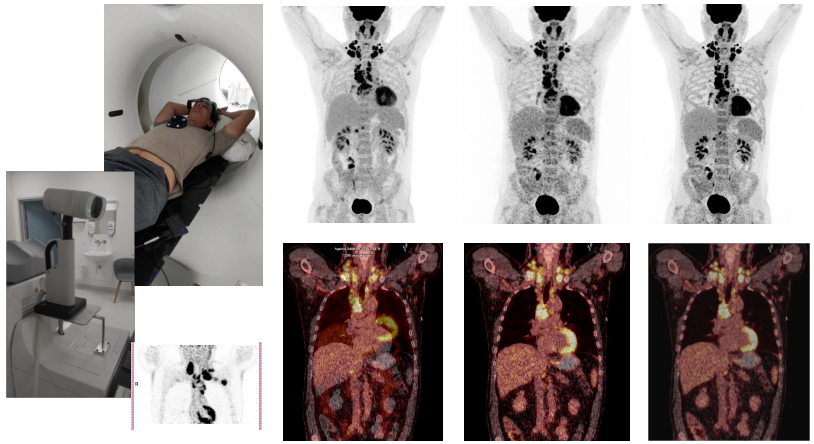
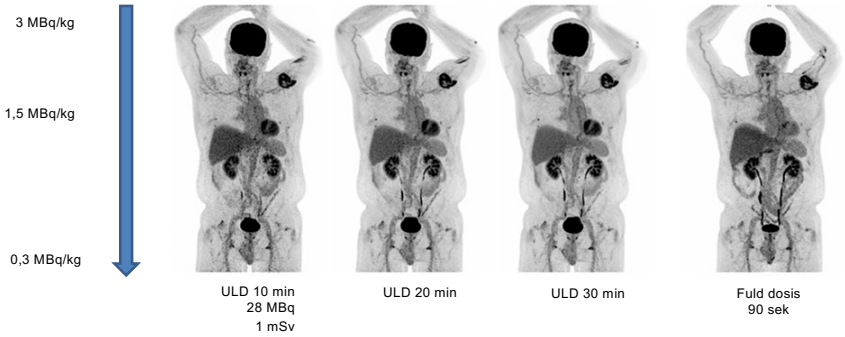
Standard 90 sek

15 sek DIBH

4x15 sek



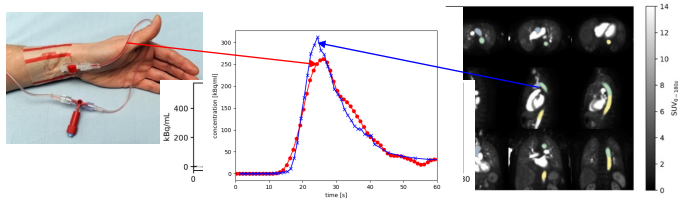
66



ULD = Ultra Low Dose

67

Non-invasive arterial-blood curve for kinetic modelling



Blood from arterial canula

Input function from imaging

- PET skanners: limited resolution – also related to time
- Quadra: High spatial and time resolution

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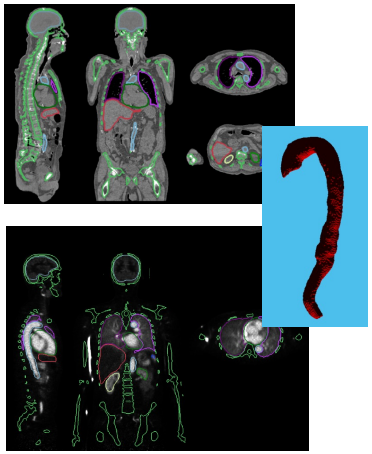
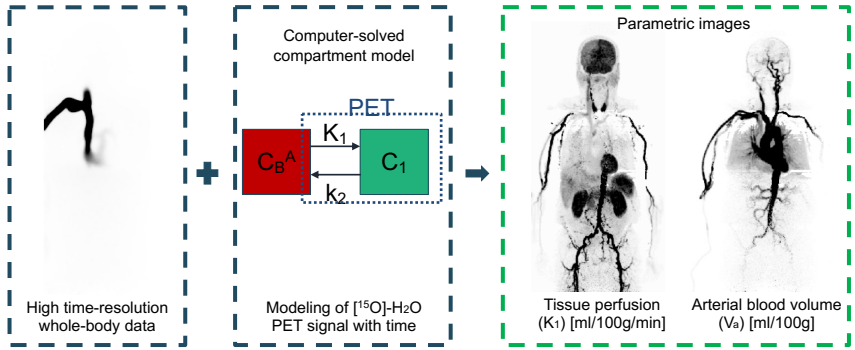
Segmentation and regions of interest



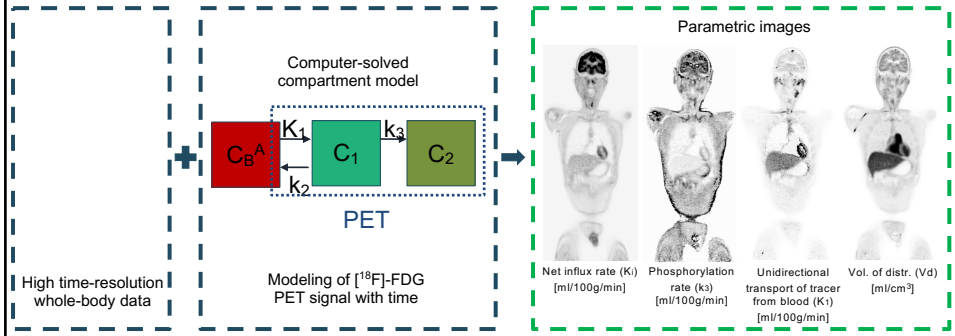
AI-based wholebody segmentation

- Aorta for non-invasive blood concentrations
- Organs
  - Quantitative tissue-time activity curves with high resolution
  - Individual organ modelling

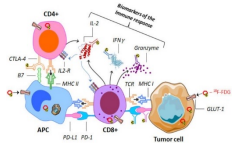
New possibilities – whole-body perfusion with [^{15}O]-H_2O



Decomposition of PET signal – kinetic modelling of [^{18}F]-FDG



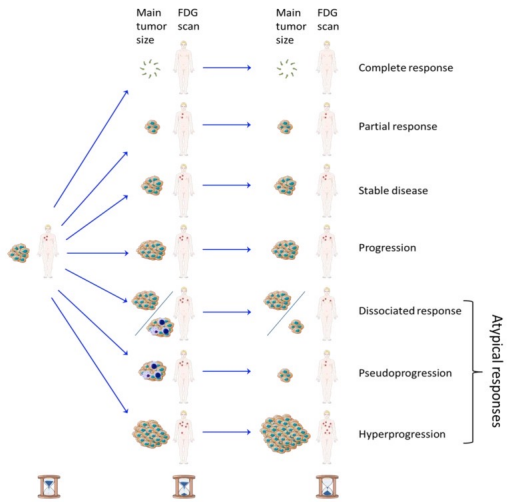
Immun check point inhibitor terapi



Reestablish immune cells' abilities to fight cancer cells - malignt melanoma, NSCLC, bladder.

FDG is taken up by both tumor and immune cells. Specific tracers to activated immune cells.

Few clinical studies and many tracers.



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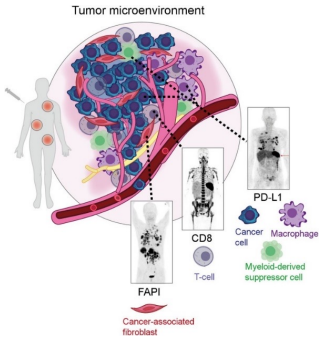

Tumor micro-environment

Cancer-associerede fibroblaster (FAP inhibitor [FAPI]), CD8-positive T-celler, CD4-celler, Programmed Death ligand 1 (PD-L1).

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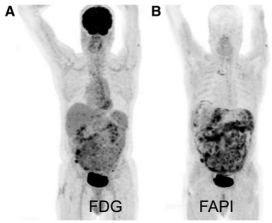
FAPI PET/CT: Will It End the Hegemony of ^{18} F-FDG in Oncology?

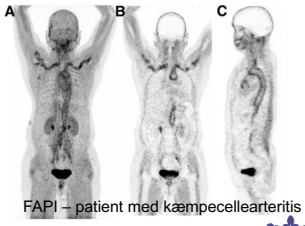
FAPI tracers low uptake in normal tissue and high in cancer.

FAPI with Ga-68, Cu-64, F-18, Tc-99m and several molecules.

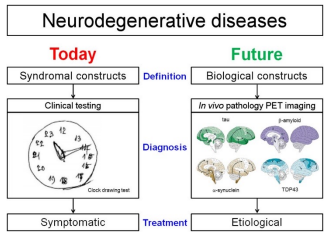
Signal-noise ration promising for AI solutions.



FDG FAPI



FAPI – patient med kæmpecellearteritis

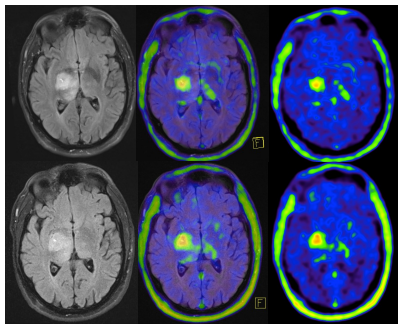


Alzheimer – from syndrom to etiology –
PET tracers for amyloid, tau etc.

Effective targeted therapy with PET
as *companion diagnostics*.
Aducanumab + 14 other drugs coming .

Other neuro-degenerative diseases
Like PE2i tracer for Parkinson's.

EANM/EANO/RANO practice guidelines/SNMMI procedure standards for imaging of gliomas using PET with radiolabelled amino acids and [^{18}F]FDG.



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Chikldren with neuroblastoma in the CNS

Median survival 6 months.

Study MSKCC with Omburtamab median survival first 93 children 47 months.

I-131 Omburtamab (monoclonal antibody) in CSF.

Binds to tumor cells behind the intact blood-brain barrier.

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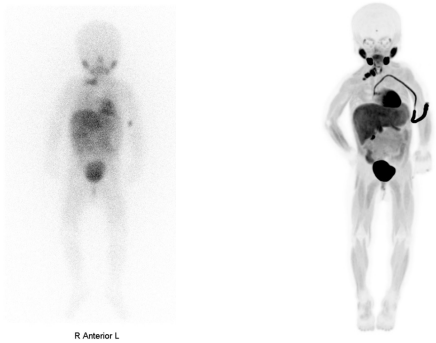

First MFBG-scan in QUADRA Total Body PET/CT. Girl 16 months with cervical neuroblastoma, 10 min. protokol without sedation or GA, breast feeding and a nap.

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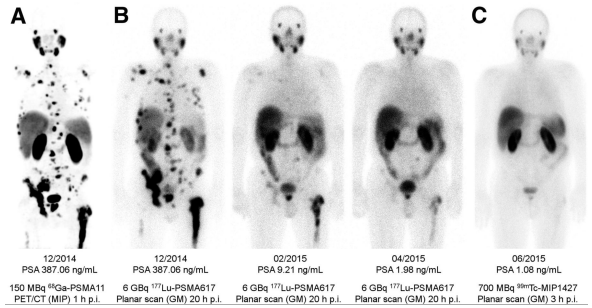
Treatment with PSMA



PSMA-Targeted Radionuclide Therapy of Metastatic Castration-Resistant Prostate Cancer with ^{177}Lu-Labeled PSMA-617

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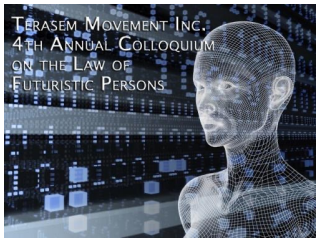
The future
– AI for imaging



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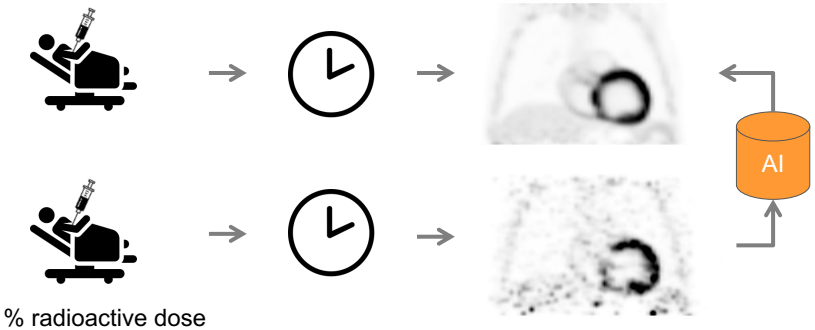
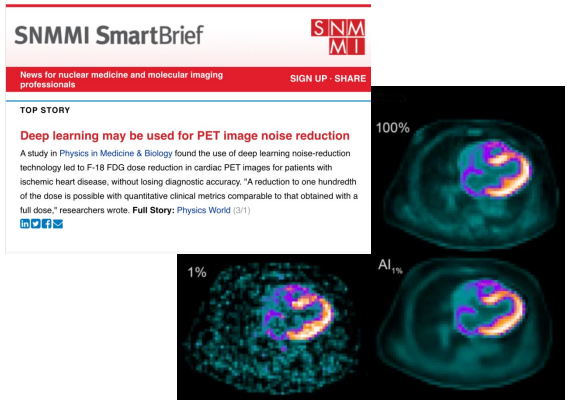
Low radiation dose

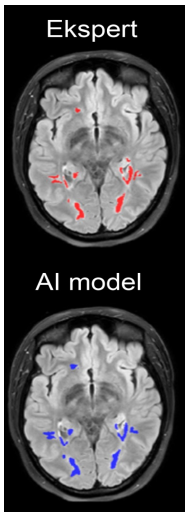


1% radioactive dose

82



Ladefoged et al, Phys Med Biol 2021 66(5), 054003



AI for Automatic analysis


ORIGINAL ARTICLE

Assessment of Artificial Intelligence Automatic Multiple Sclerosis Lesion Delineation Tool for Clinical Use

Amalie Monberg Hindsholm[1] · Stig Præstekjær Cramer[1] · Helle Juhl Simonsen[1] · Jette Lautrup Frederiksen[2] · Flemming Andersen[1] · Liselotte Højgaard[1] · Claes Nøhr Ladefoged[1] · Ulrich Lindberg[1]

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The futuristic perspective

All persons have their own digital twin in the ”sky”, and have annual US/PET/CT/MR + blood tests with ”genomics” and other ”omics”, epigenetics ”liquid biopsy” for tumor cell-DNA.

AI compares results with the digital twin in the sky from last year, and Suggests a treatment plan with personalized medicine.

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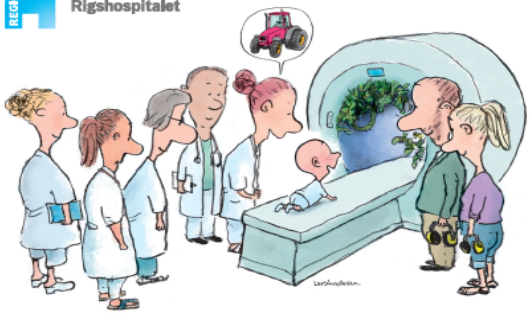
Rigshospitalet



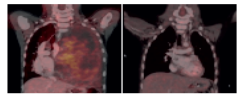
Leg lokkede den lille kræftpatient ind i MR-scanneren

Liselotte Højgaard, klinikchef, professor, dr.med., Lise Borgwardt, overlæge, ph.d. og overlæge Helle Hjorth Johannesen, Klinik for Klinisk Fysiologi, Nuklearmedicin og PET, Rigshospitalet

I foråret 2019 havde vi på Rigshospitalet en lille patient; en meget syg dreng på 4 år. Han var tidligere ræk, men havde udviklet en stor kræftsvulst i venstre lunge. Så stor, at hjertet, der normalt sidder i venstre side, var skubbet helt over i højre side og op mod halsen.

sien ikke bedøve drengen – de mente at han ville kunne gå til, hvis han blev lagt ned og kom i narkose/fik noget at sove på. Og uden billeder kunne operationen ikke laves. Så alle stod med ryggen mod muren.

Drengen var meget fornuftig og havde fanta-



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