



Faculty of Health Sciences



# PET/CT and PET/MRI

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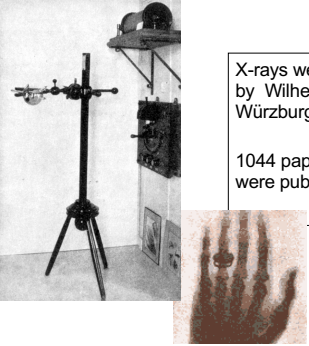
Liselotte Højgaard (1957), MD 1982, specialist clinical physiology & nuclear medicine.

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.


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The first X-ray machine Copenhagen 1896

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### Nuclear Medicine was born in Copenhagen



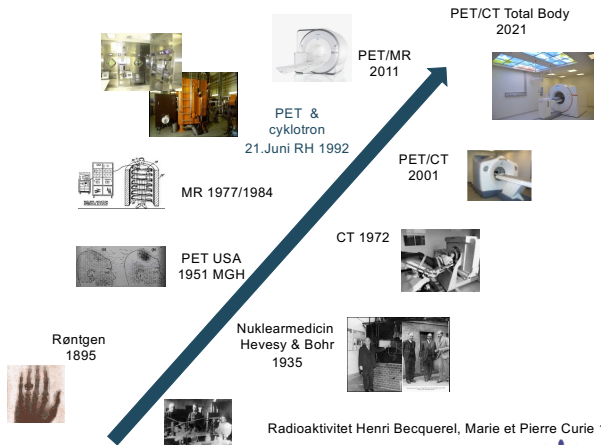
Nuclear Medicine was developed in Copenhagen by Georg de Hevesy & Niels Bohr and published in 1935.

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

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PET/CT Total Body 2021

PET/MR 2011

PET & cyklotron 21. Juni RH 1992

PET/CT 2001

MR 1977/1984

CT 1972

PET USA 1951 MGH

Nuklearmedicin Hevesy & Bohr 1935

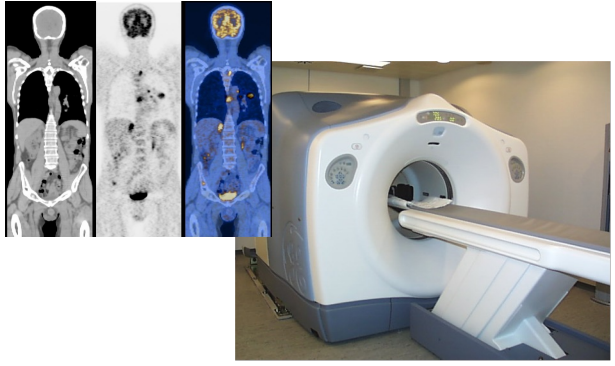
Radioaktivitet Henri Becquerel, Marie et Pierre Curie 1903

Röntgen 1895

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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

**PET/CT**

DTU **Ultrasound** **CT** **MR** **RH**

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

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## Many diseases, many methods, which one ?

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

**PET/CT**

DTU **Ultrasound** **CT** **MR** **RH**

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**PET** positron emission tomography      **CT** computer tomography

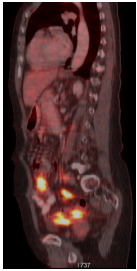
Annihilation      Gamma rays 511 KeV

*F-18 FDG: fluoro-deoxyglucose is a glucose analogue, showing glucose metabolism. 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 metabolism
- Oncology: staging, treatment effect, relapse, control, RTP- and OP-planning

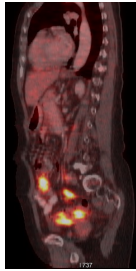
35,000 publications on PET



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## PET/CT as first line imaging

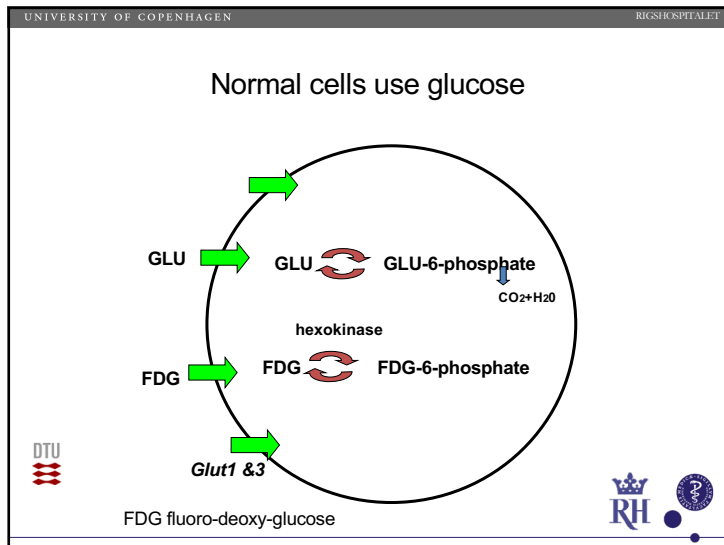


PET/CT with FDG is integrated in Danish routine patient work up "Kræftpakkerne"

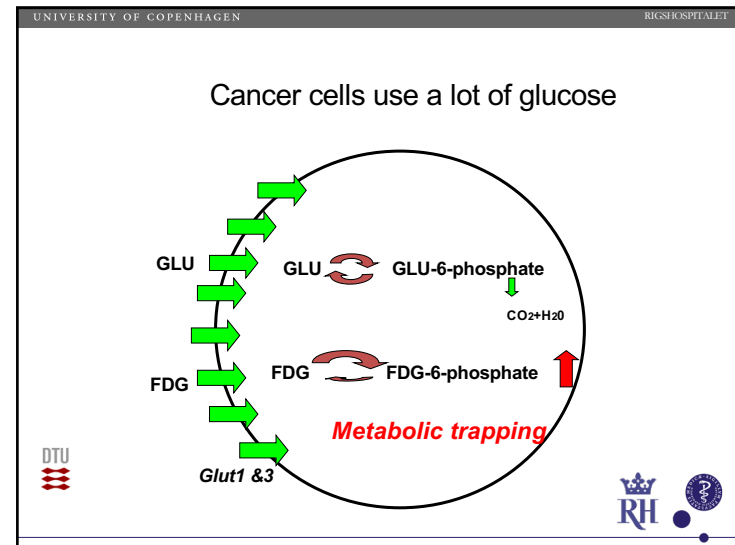
- Brain tumors
- Lung cancer
- Cervical and ovarian cancer
- Lymphoma
- Head & Neck
- Gastro-intestinal
- Sarcomas
- Malignant melanoma



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

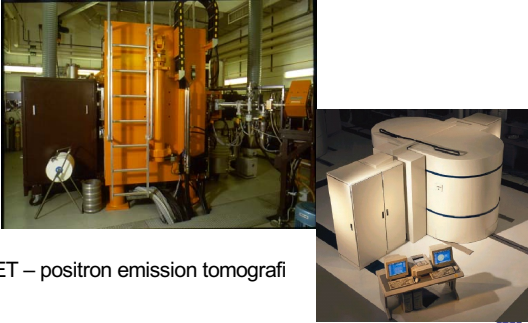
**FDG: F-18 flouro-deoxy-glucose**

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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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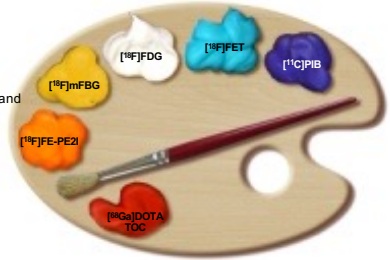
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### Tracers for PET

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-HT <sub>2A</sub> receptors
[C-11] CUMI-101	5-HT <sub>1A</sub> receptors
[C-11] DASB	Serotonin transporter
[C-11] Flumazenil	Central benzodiazepin receptor
[C-11] PIB	beta-amyloid plaques
[C-11] SB207145	5-HT <sub>4</sub> receptors
[O-15] H <sub>2</sub> O	Brain CBF
[N-13] NH <sub>3</sub>	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

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Cyklotrons – small 2-3 MeV deuteron-machines <sup>15</sup>O-vand  
 230 - 400 MeV superconducting magnets for particle-therapy  
 And research in high energy physics (CERN, RIKEN, iThemba).

**<sup>18</sup>F, <sup>11</sup>C, <sup>13</sup>N og <sup>15</sup>O og <sup>64</sup>Cu, <sup>89</sup>Zr, <sup>124</sup>I.** Isotopes for PET-tracers

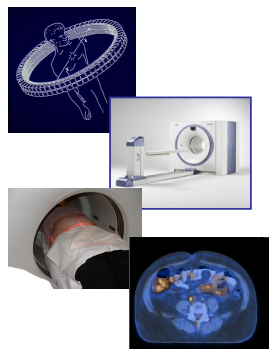
- Increasing demand
- Different tracers
- Focus on security, GMP, supply chain stability, flexibility, research
- Alfa-therapy for theranostics: ligand with **Astatin-211 for treatment, Actinium-225 for diagnosis with PET scan**

Tak til Holger Jensen 


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**”PET - The fastest growing medical technology ever ”**



- Positron tracer F-18 FDG
- Patient injection
- PET scanning combined with CT
- Interpretation by NM & radiologist

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

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**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

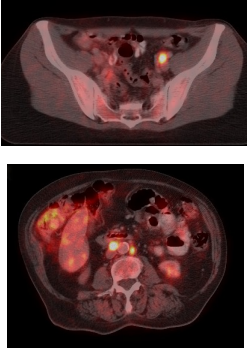
- non commercial
- private-public partnership
- industry driven

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### PET/CT in cervical cancer



Metastatic lymph nodes:

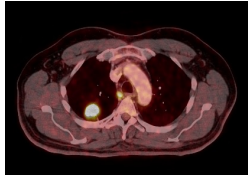
- Pelvis
- Para-aortal
- Inguinal
- Mediastinum
- Neck
- Omentum

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### 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.

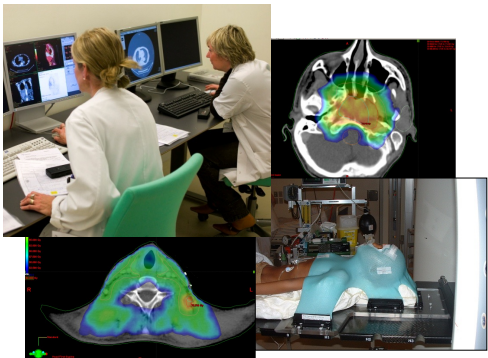
Relative risk reduction for a futile thoracotomy 51 %.

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

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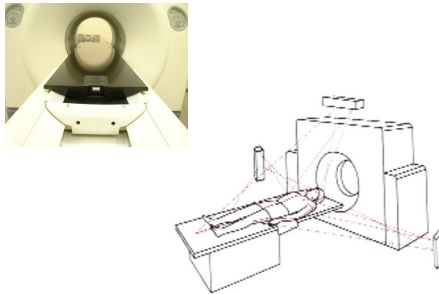


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### External LAP laser system







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### PET/CT for planning of radiation therapy



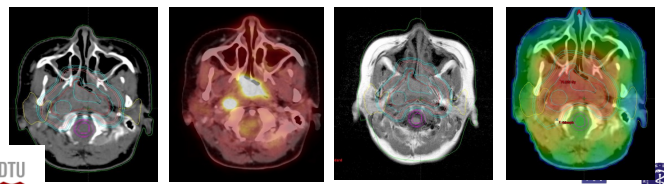
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### Radiotherapy and imaging


Radiotherapy planned by CT  
 If tumor is drawn too small possibilities for cure smaller  
 If tumor is drawn too large side-effects worse  
 PET and MRI to improve methodology






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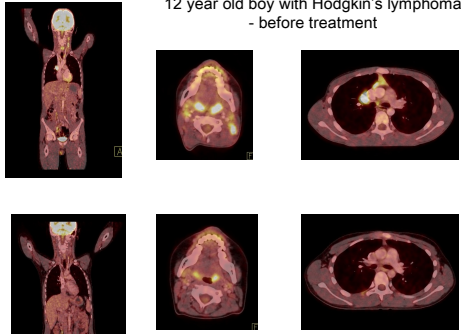
### Advance PET scanner 1995




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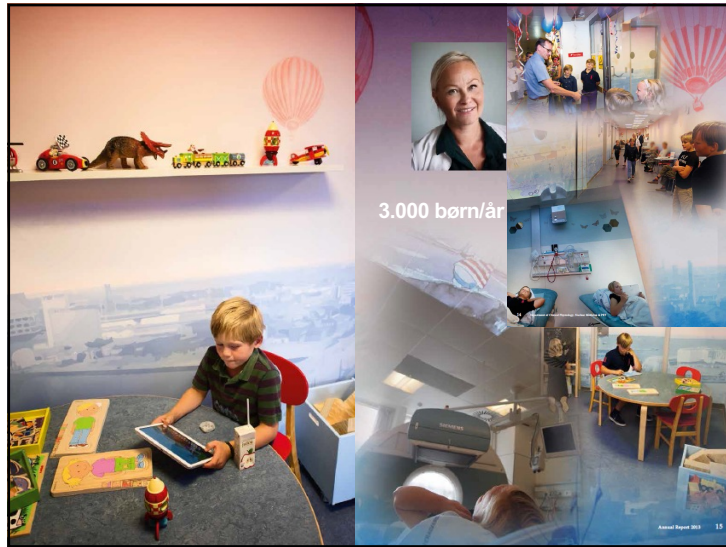
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12 year old boy with Hodgkin's lymphoma - before treatment



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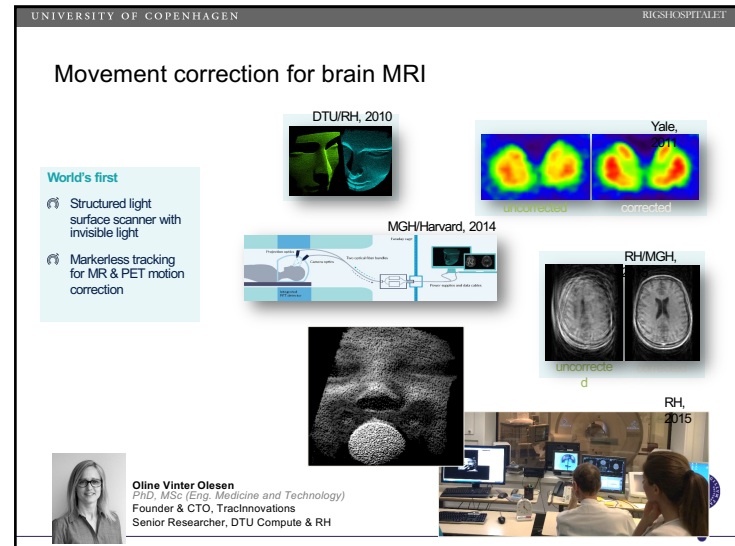
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### Cluster for molecular imaging



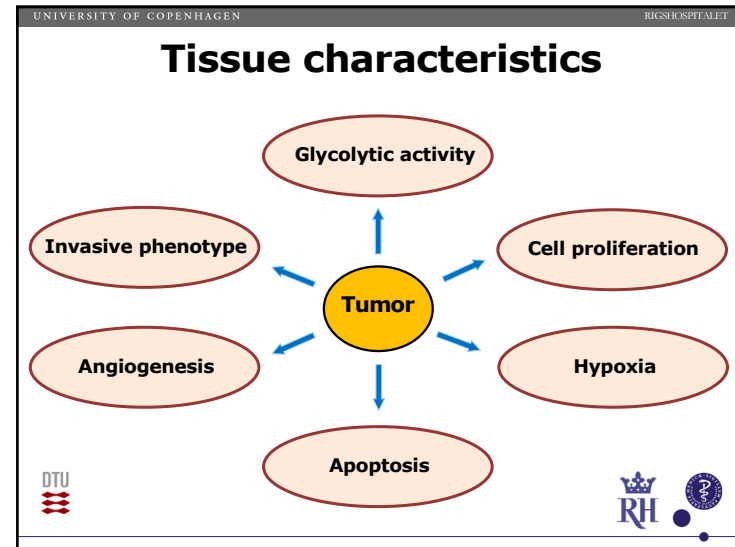
Development of new tracers .

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

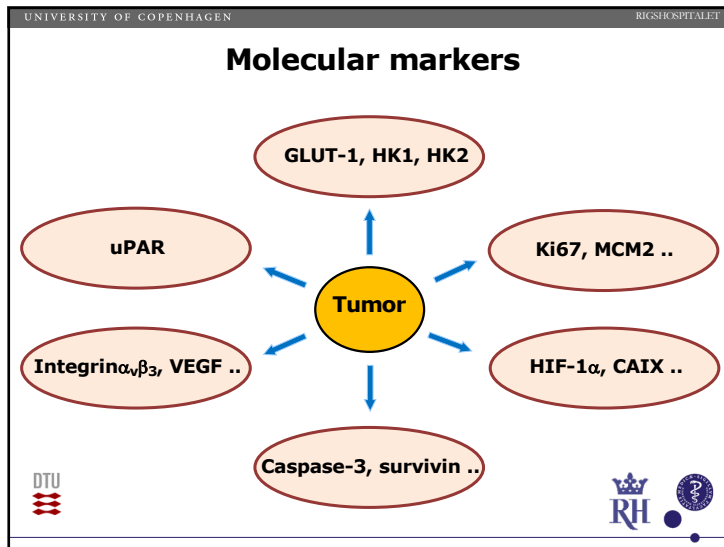
Translational from use in animal to man.

DTU The Danish National Advanced Technology Foundation RH

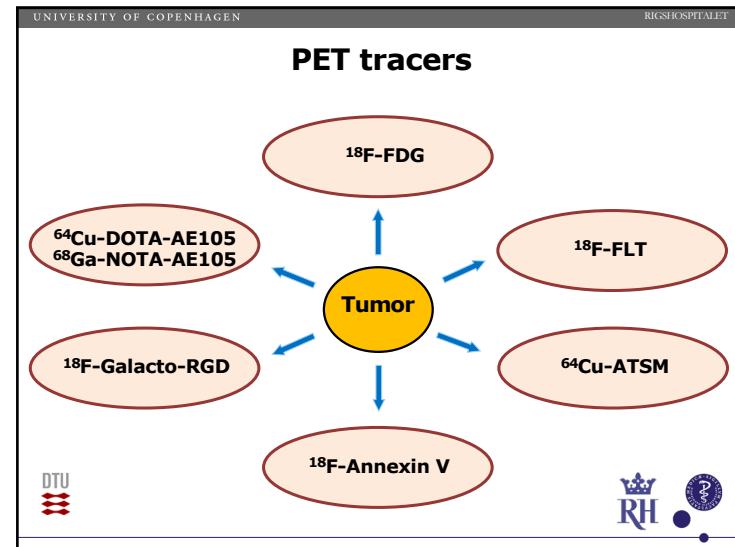
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### uPAR-PET/MRI of brain cancer – from mouse to man

**PDOX GBM** **GBM**

A H&E B uPAR C Autoradiography

Normal brain Cancer cells Normal brain uPAR

**Ex vivo target validation**

Prof. Andreas Kjaer et al.

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

#### Copenhagen PET/MRI

- Simultaneous PET and MRI
- From December 2011

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

MR

PET

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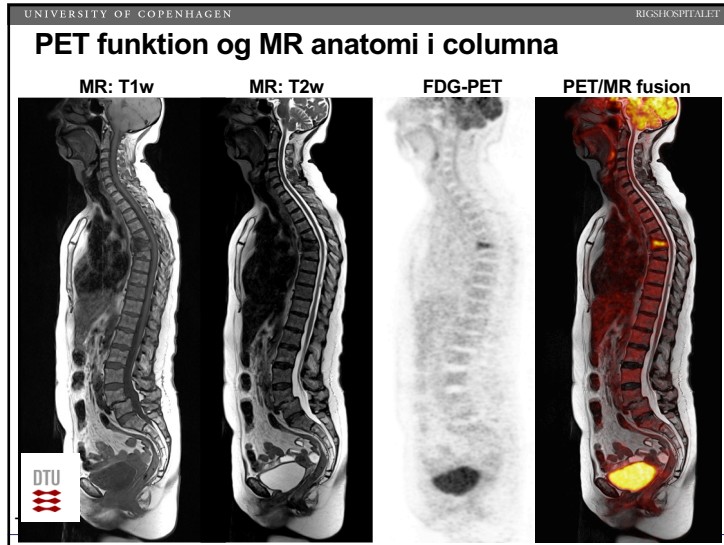
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### FDG-PET

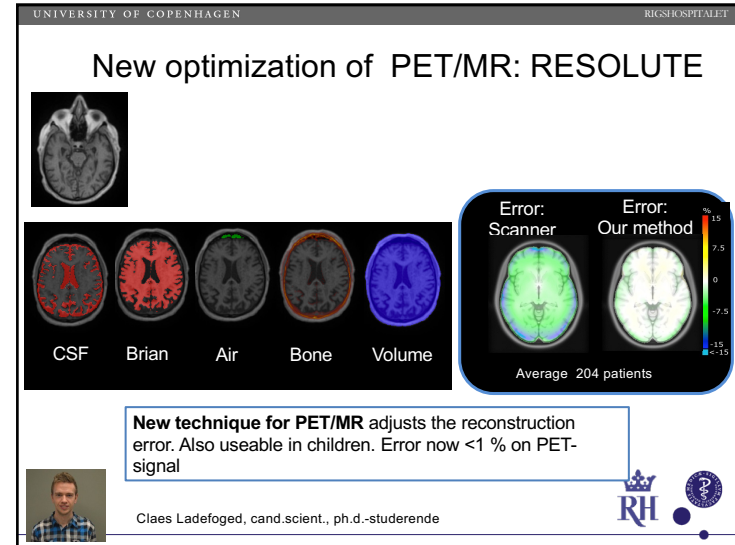
### MR: T2w

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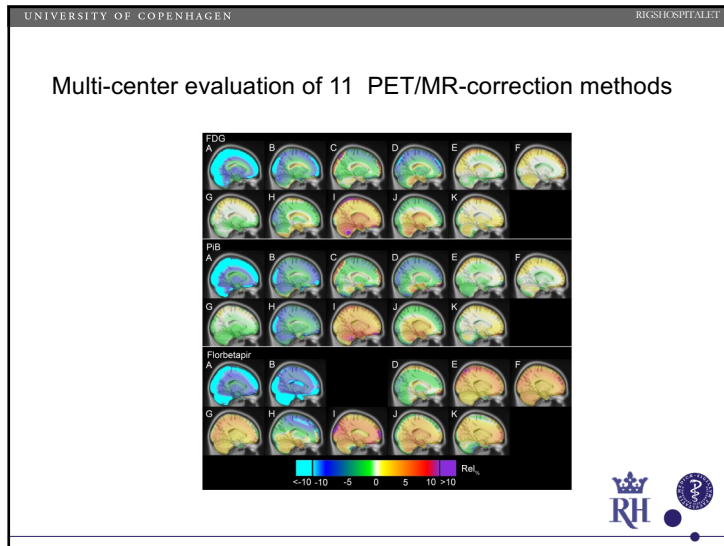




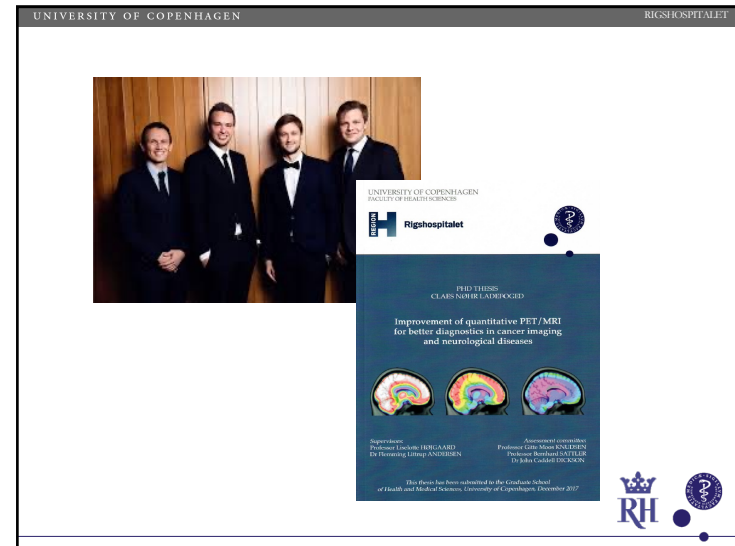
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## AI for better imaging



- 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 ???

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CADI

Lavere stråledosis / Kortere scantid

Automatisk indtegning

Beslutningsstøtte

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Idea, projekts, AI – research lab

AI research

Clinical research with validation on independent Data set

Clinical use

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### Clinical practice brain studies

T1 MRI

18F-FE-PE2I DaT PET

18F-FDG PET/MR

Hippocampal delineation- Anterior to posterior

R L

Hippocampal Volume


Alzheimer's

18F-FET PET

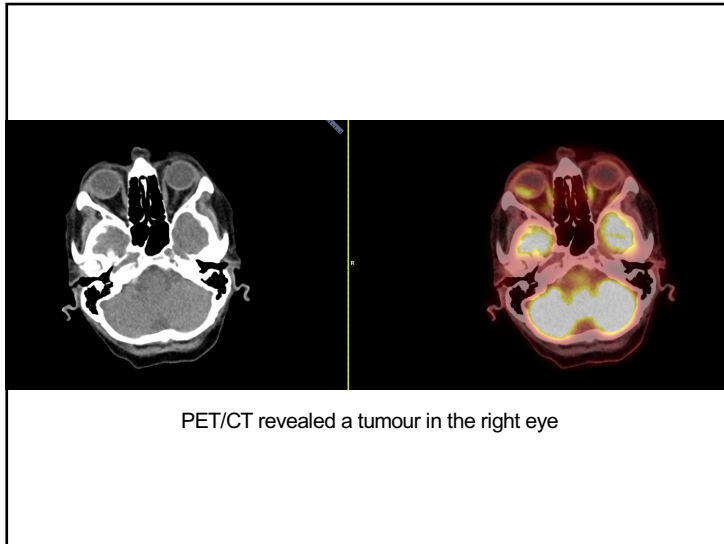
Recurrent Glioblastoma

Parkinson's Disease

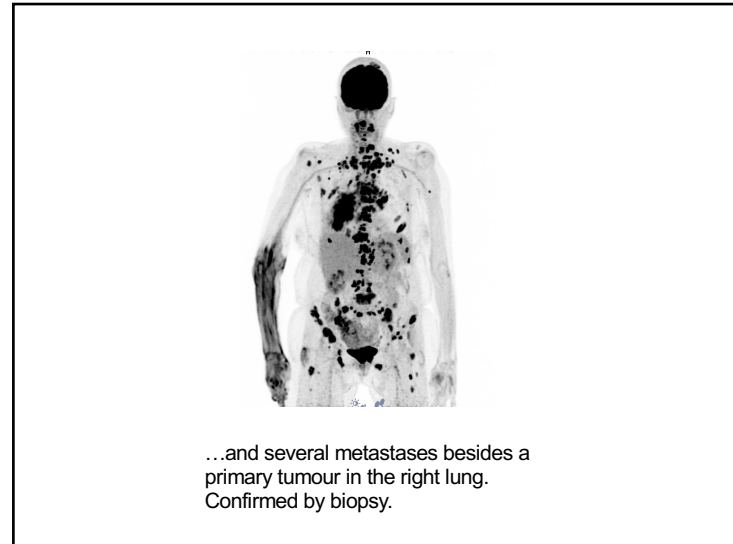
Prof. Ian Law



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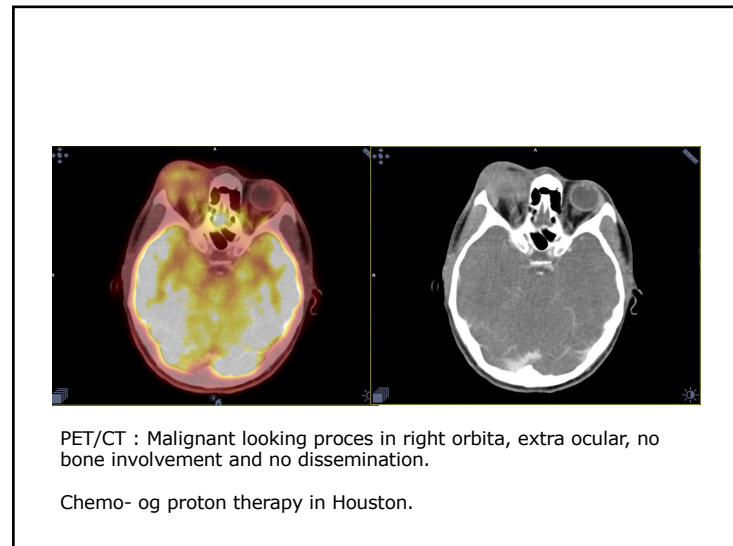


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12 year old boy, previously well, swelling of the right eye. MRI local hospital: proces in right orbita around bulbus.

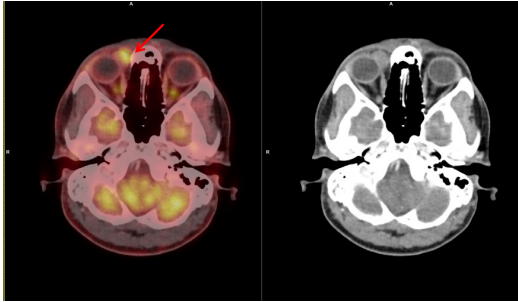
Normal vision. Biopsy: embryonal rhabdomyosarkoma. WB FDG PET/CT for staging.

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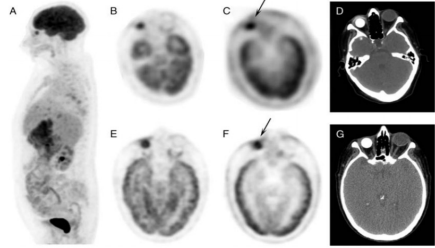
1 year later suspicion of relapse of the rhabdomyosarcoma in the right orbita at control MRI. Referred to WB FDG PET/CT for metabolism in tumor and dissemination ?



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

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

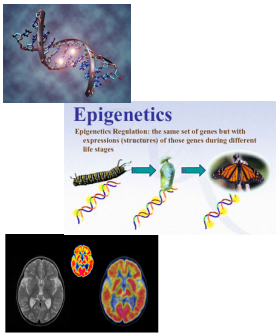


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**Personalised Medicine**



**Epigenetics**  
Epigenetics (regulation) - the same set of genes but with expressions (structures) of those genes during different life stages

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

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

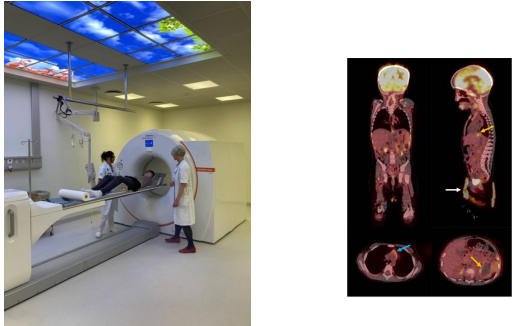

*"Couldn't I get the something else right away?"*



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### QUADRA Total body PET/CT

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

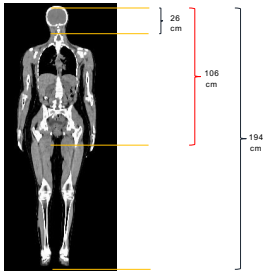
Long field-of view to physiologi & patophysiologi  
with kinetics from dynamic acquisitions - total body  
system-physiologi.

*Deep inspiration breath hold for planning of  
radiotherapy.*





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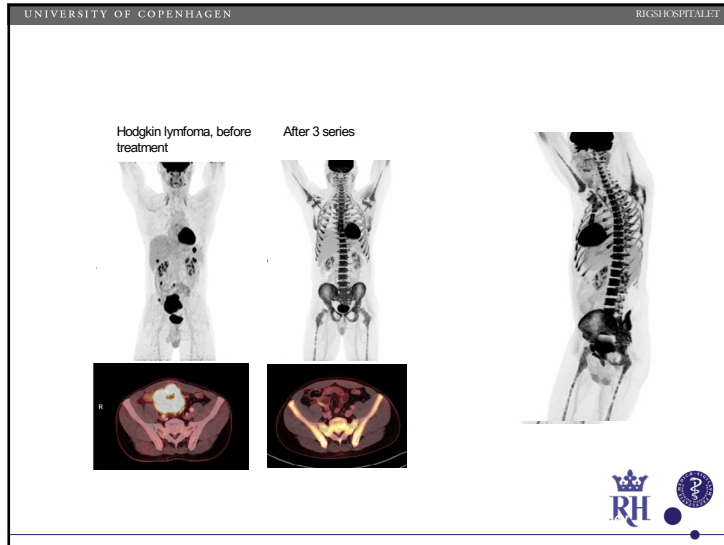


Sensitivity:  
x 10 standard digital scanner  
x 40 analog scanner

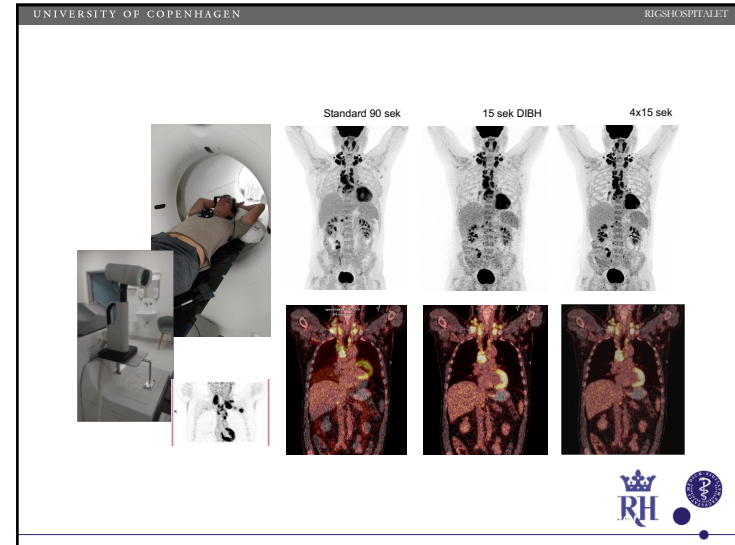
3.2-mm krystal Vision teknologi

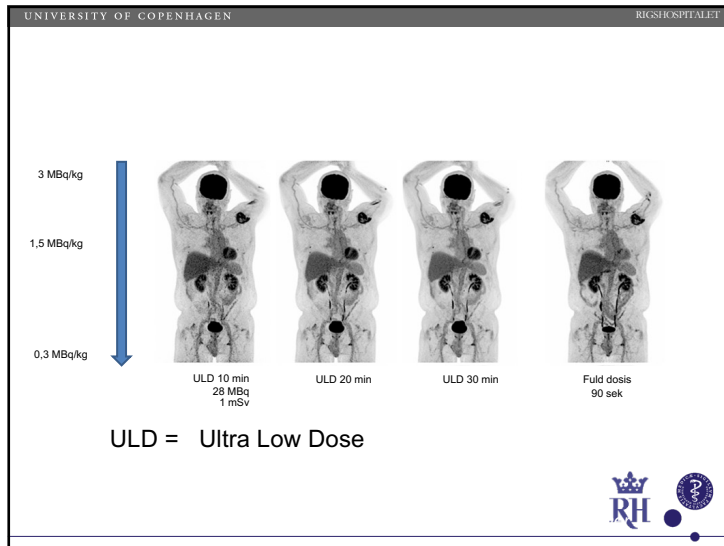
64



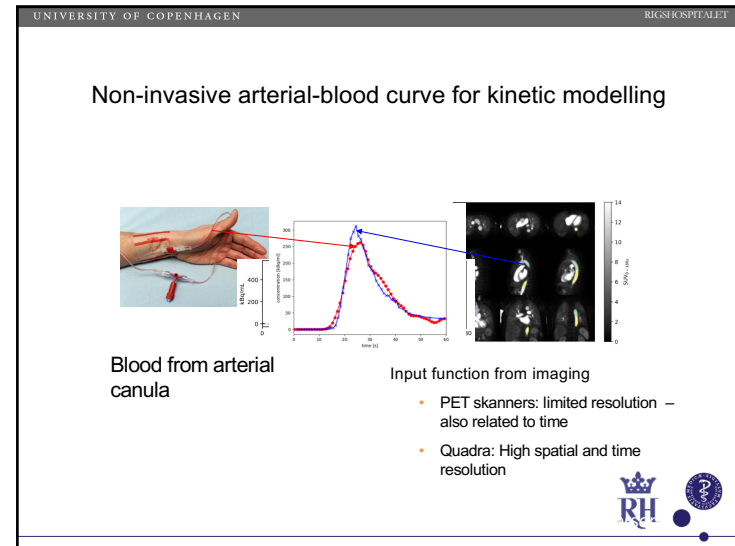
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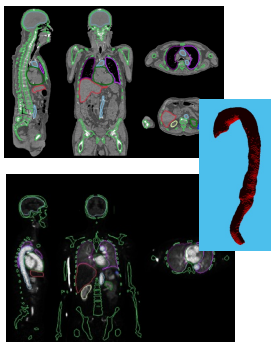


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### Segmentation and regions of interest



AI-based wholebody segmentation

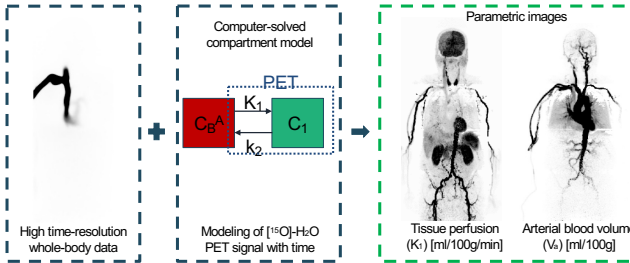
- Aorta for non-invasive blood concentrations
- Organs
  - Quantitative tissue-time activity curves with high resolution
  - Individual organ modelling

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### New possibilities – whole-body perfusion with $[^{15}\text{O}]\text{-H}_2\text{O}$



High time-resolution whole-body data

Computer-solved compartment model

PET

$C_{B^A}$   $C_1$

$K_1$   $k_2$

Modeling of  $[^{15}\text{O}]\text{-H}_2\text{O}$  PET signal with time

Parametric images

Tissue perfusion ( $K_1$ ) [ml/100g/min]

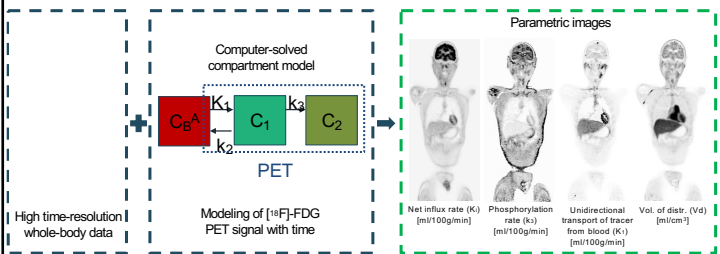
Arterial blood volume ( $V_A$ ) [ml/100g]

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



High time-resolution whole-body data

Computer-solved compartment model

PET

$C_{B^A}$   $C_1$   $C_2$

$K_1$   $k_2$   $k_3$

Modeling of  $[^{18}\text{F}]\text{-FDG}$  PET signal with time

Parametric images

Net influx rate ( $K_1$ ) [ml/100g/min]

Phosphorylation rate ( $k_3$ ) [ml/100g/min]

Unidirectional transport of tracer from blood ( $K_1$ ) [ml/100g/min]

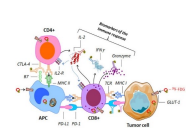
Vol. of distr. ( $V_d$ ) [ $\text{ml}/\text{cm}^3$ ]

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### Immun check point inhibitor terapi



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

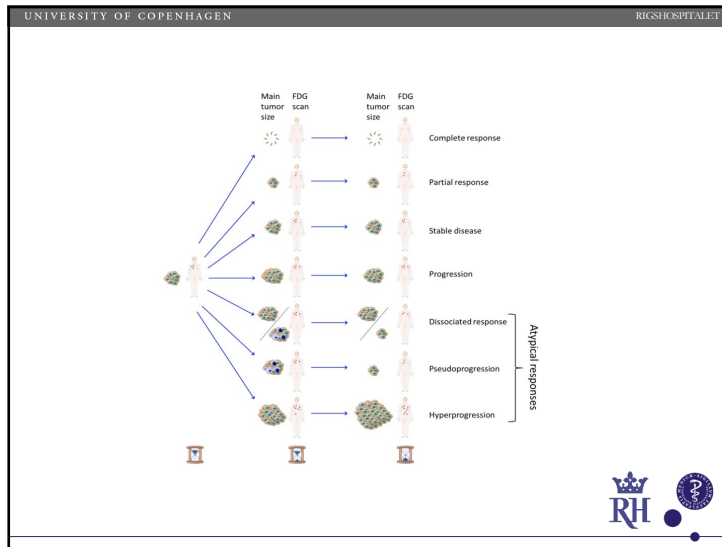
FDG is taken up by both tumor and immune cells. Specific tracers to activated immune cells.

Few clinical studies and many tracers.

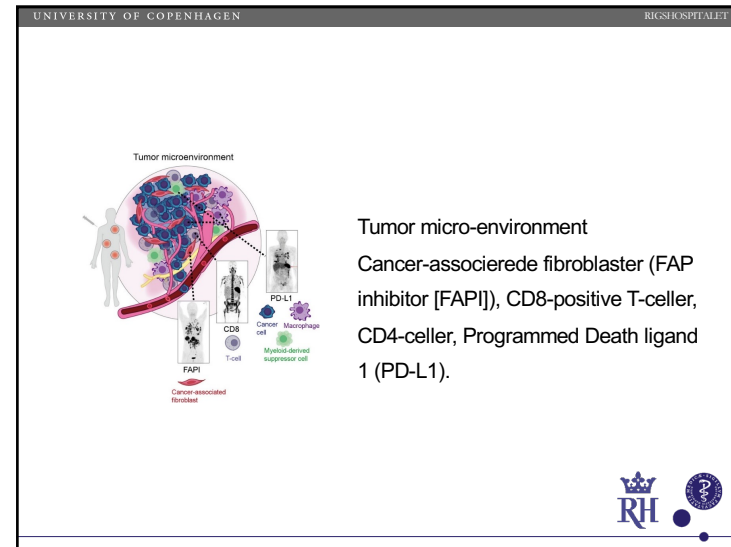
RH

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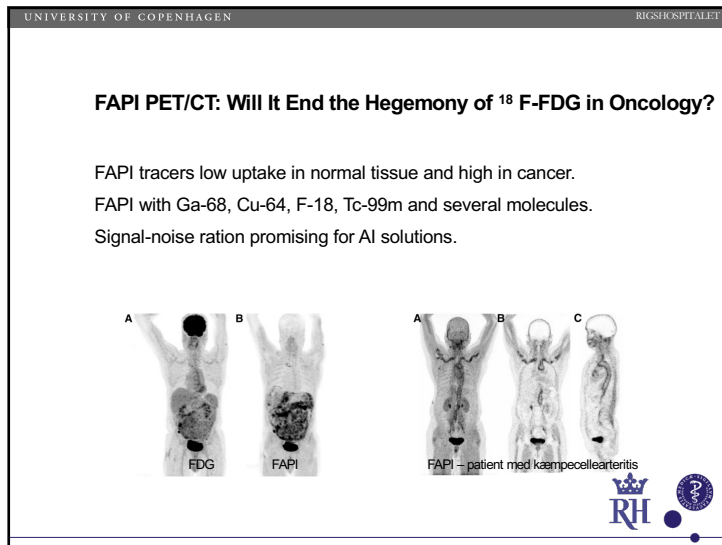




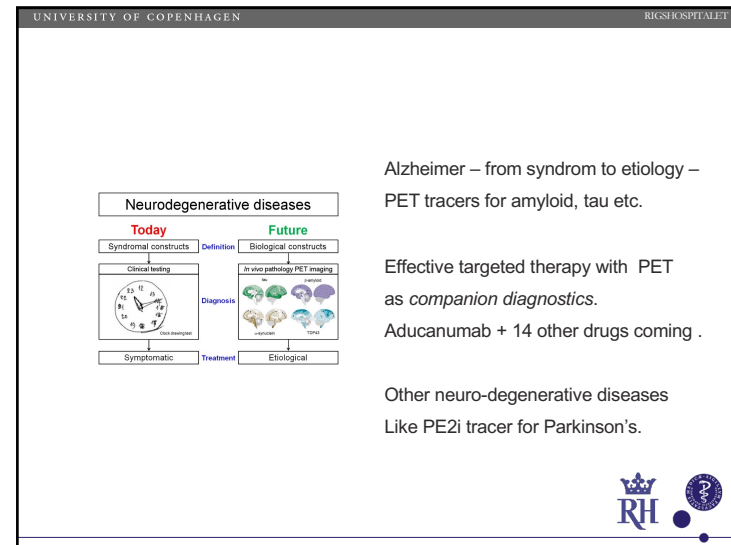
73



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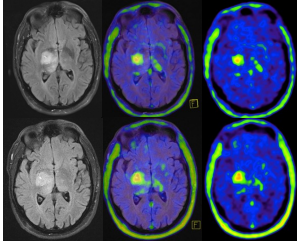
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EANM/EANO/RANO practice guidelines/SNMMI procedure standards for imaging of gliomas using PET with radiolabelled amino acids and [<sup>18</sup>F]FDG.



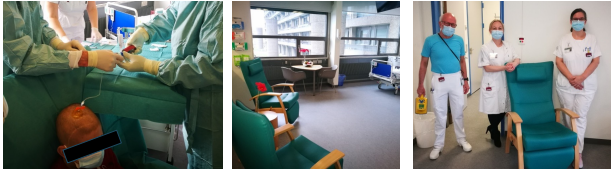
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### Children with neuroblastoma in the CNS

Median survival 6 months.  
Study MSKCC with Omburtamab median survival first 93 children 47 months.

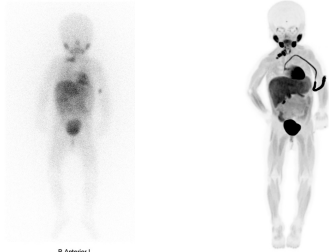


I-131 Omburtamab (monoclonal antibody) in CSF.  
Binds to tumor cells behind the intact blood-brain barrier.

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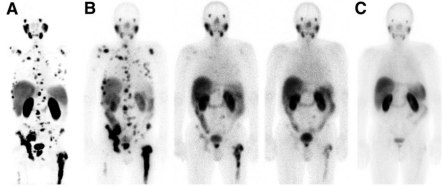
First MFBG-scan in QUADRA Total Body PET/CT. Girl 16 months with cervical neuroblastoma, 10 min. protokol without sedation or GA, breast feeding and a nap.

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### Treatment with PSMA



12/2014 150 MBq <sup>109</sup> Cs-PSMA11 PET/CT (MPI) 1 h p.i.	12/2014 PSA 387.00 ng/mL 6 GBq <sup>177</sup> Lu-PSMA617 Planar scan (GM) 20 h p.i.	03/2015 PSA 9.21 ng/mL 6 GBq <sup>177</sup> Lu-PSMA617 Planar scan (GM) 20 h p.i.	04/2015 PSA 1.98 ng/mL 6 GBq <sup>177</sup> Lu-PSMA617 Planar scan (GM) 20 h p.i.	06/2015 PSA 1.28 ng/mL 700 MBq <sup>177</sup> Lu-MIP1407 Planar scan (GM) 3 h p.i.
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PSMA-Targeted Radionuclide Therapy of Metastatic Castration-Resistant Prostate Cancer with <sup>177</sup>Lu-Labeled PSMA-617

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# The future – AI for imaging



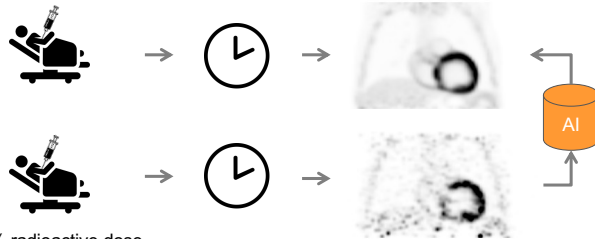
TERASEM MOVEMENT INC.  
4TH ANNUAL COLLOQUIUM  
ON THE LAW OF  
FUTURISTIC PERSONS




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# Low radiation dose

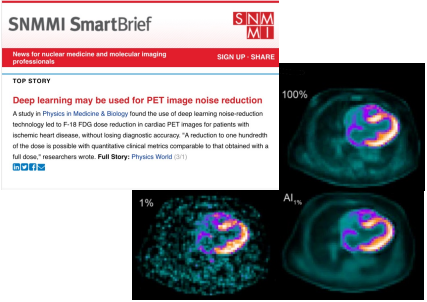


1% radioactive dose



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SNMMI SmartBrief

News for nuclear medicine and molecular imaging professionals SIGN UP - SHARE

TOP STORY

Deep learning may be used for PET image noise reduction


A study in Physics in Medicine & Biology found the use of deep learning noise-reduction technology led to F-18 FDG dose reduction in cardiac PET images for patients with ischemic heart disease, without losing diagnostic accuracy. "A reduction to one hundredth of the dose is possible with quantitative clinical metrics comparable to that obtained with a full dose," researchers wrote. Full Story: Physics World (1)

100%

1%

AI

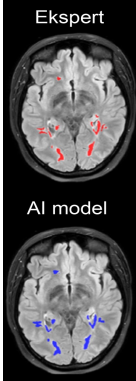

Ladefoged et al, Phys Med Biol 2021 66(5), 054003



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# AI for Automatic analysis





ORIGINAL ARTICLE

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

Amalie Monberg Hindsholm · Stig Præststøl Cramer · Helle Juhl Simonsen · Jette Laurrup Frederiksen · Flemming Andersen · Liselotte Højgaard · Claes Nohr Ladefoged · Ulrich Lindberg


Received 2 June 2021 / Accepted 18 August 2021  
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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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LEDDEN RIGSHOSPITALET



## Leg lokkede den lille kræftpatient ind i MR-scanneren

Liselotte Højgaard, kliniskchef, 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 rolig dreng på 4 år. Han var tidligere medicineret, men havde udviklet en stor kræftvulst i venstre lunge. Så stod et hjerte, der normalt sidder i venstre side, var akubt bilet helt over højre side og op mod halsen.

Den lille dreng havde en meget fornuftig og havde fantasien ikke bedøvet drengen – de mente at han ville kunne gå til, hvis han blev lagt ned og kom i ro. Så fik meget 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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