

# Radiotherapy during pregnancy



1. Current clinical practice & data

2. Dosimetry in pregnancy radiotherapy

3. Potential benefit from advanced radiotherapy

4. EURADOS activities & plans

# Clinical practice & data



# Current clinical practice

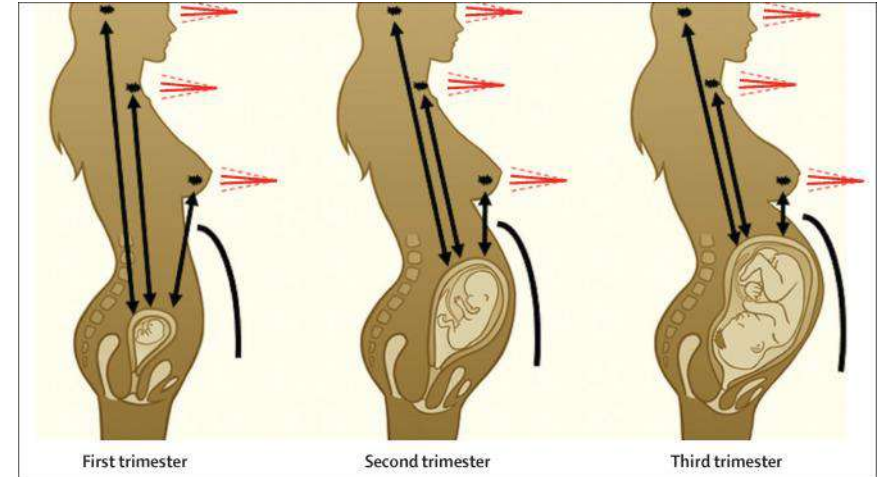
- 1 in 1000 pregnancies are complicated with cancer
- More than 70% of patients are treated during pregnancy
- Radiotherapy is only applied in 3% of the cases
  - Mostly breast (54%) and brain cancers (15%)
  - In first trimester can be an alternative to chemotherapy avoiding treatment delays
  - Generally radiotherapy is postponed till after delivery
- Radiotherapy during pregnancy treated as a prohibited topic
  - Lack of reliable information on the risk of fetal damage
  - Lack of data on the dose to the fetus during pregnancy
  - What dose is considered allowed?
    - ICRP - Threshold for deterministic effects (e.g. malformations) 100-200 mGy
    - Generally a threshold of 100 mGy is used
    - No threshold for risk of cancer

Stage of pregnancy	Therapeutic options
First trimester	Surgery
	Radiotherapy
Second trimester	Surgery
	Radiotherapy
	Chemotherapy
Third trimester	Surgery
	Chemotherapy

F. Amant, et al., European Journal of Cancer 2010

# General aspects of RT during pregnancy

- Fetus dose is dependent on cancer position
  - Larger the distance between tumor and fetus the better
  - Generally assumed for upper body parts RT is possible
- Fetus dose will also depend on the stage of pregnancy
  - 1<sup>st</sup> trimester is further than 2<sup>nd</sup> and 3<sup>rd</sup> trimester
  - Safe RT < 3<sup>rd</sup> trimester
- Fetal shielding is generally applied in conventional radiotherapy
  - Dose reduction factor 2-4
  - Heavy materials
    - Strong supports
      - Risks
    - Lead apron
      - Not very comfortable for patient



T Vandembroucke, et al. *The Lancet* 2017. Effects of cancer treatment during pregnancy on fetal and child development

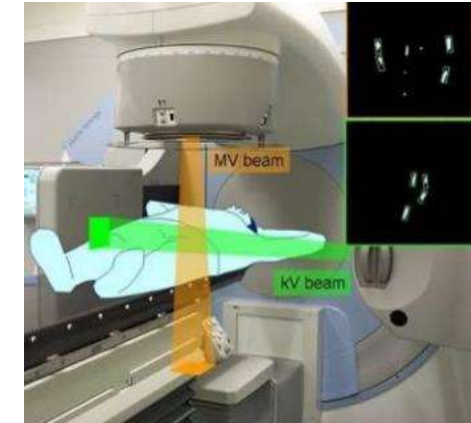
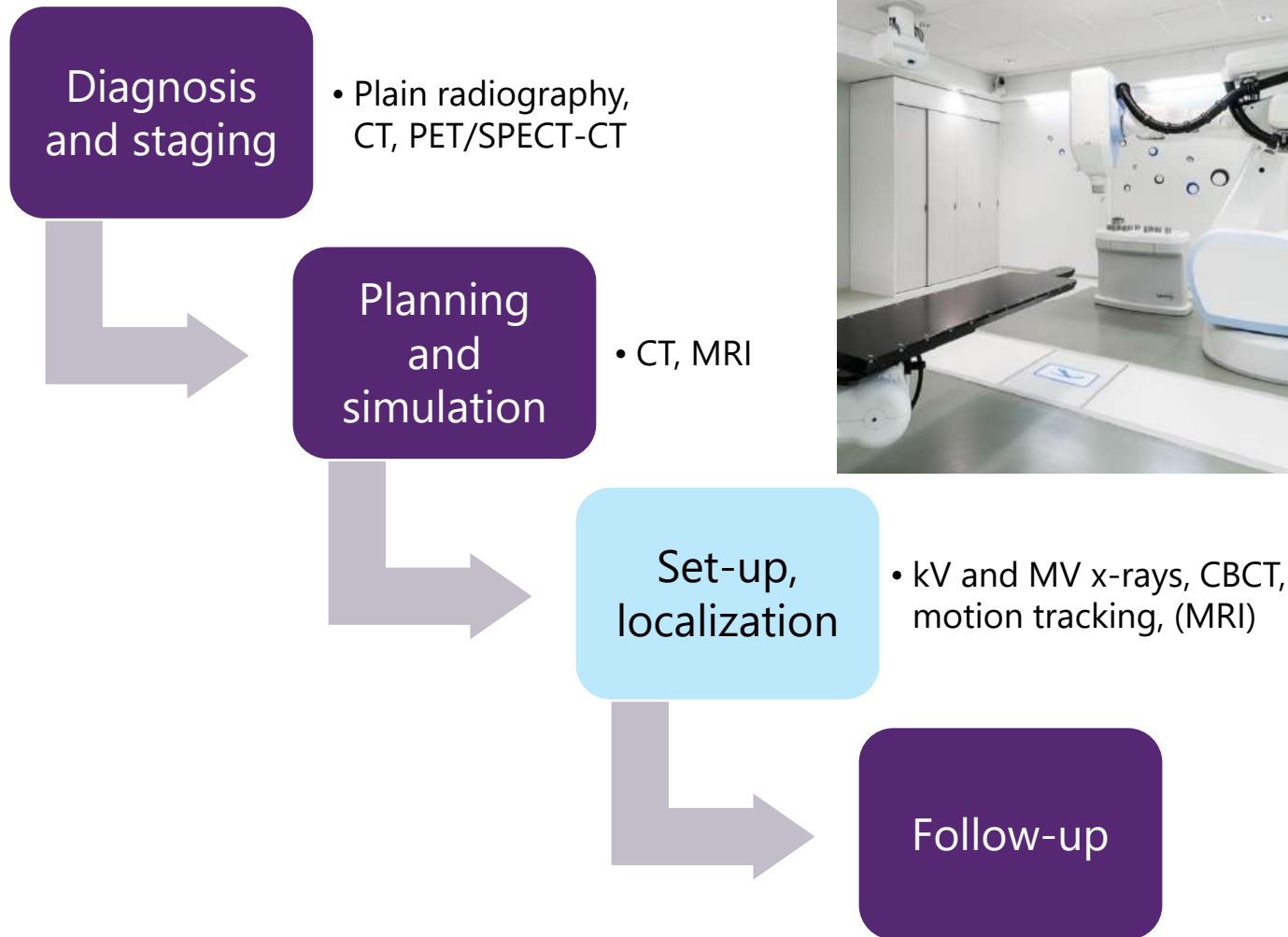


F. Amant et al. / *Best Practice & Research Clinical Obstetrics and Gynaecology* 29 (2015)



<https://www.iaea.org/resources/rpop/health-professionals/radiology/pregnant-women>

# Imaging in radiotherapy process



Highly conformal treatments are routine – target positioning is critical -> imaging at each fraction  
Image-Guided RadioTherapy

# Clinical fetus dose data

Few studies on reported fetus doses and outcome

- Review paper HB Kal et al., reporting fetus dose during pregnancy photon radiotherapy
  - Breast carcinoma: fetus dose 40-180 mGy
  - Hodgkin's disease: fetus dose 9-500 mGy
  - Brain tumours: fetus dose 3-90 mGy
- For breast and Hodgkin's disease shielding was always applied while for brain, H&N only in 1 case
- Outcomes of children are reassuring, but long-term follow-up is limited

Maternal dose (Gy)	Fetal dose (Gy)	Pregnancy trimester	n	Delivery	Ref
<b>Breast carcinoma*</b>					
50	0.160	3	1	Healthy boy	27
50	0.14-0.18	3	1		28
46	0.039	1	1	Healthy boy	29
<b>Hodgkin's disease*</b>					
35-40	0.014-0.055 (6 MV) 0.100-0.136 (cobalt)	1-3	16	Healthy babies/ no malignant disease	25
19	0.09-0.42, head 0.114	3	1	Healthy child at age 8 years	33
15-20	0.020-0.50	2-3	7	Healthy children at age 6-11 years	34
			16	Healthy babies	36
35	<0.1	2	1	Healthy child	37
<b>Brain tumours, head and neck cancer†</b>					
64	0.027-0.086	2	1	Healthy baby	33
45	0.020	1	1		41
25	0.0015-0.0031	3	1		42
30	0.003	2	1	Healthy boy at age 3 years	43
68	0.06	3	1	Healthy girl at age 2.5 years	44
78.2	0.030	3	1	Healthy girl at age 1.5 years	44
66	0.033-0.086*	3	1		45

\*With shielding. †Without shielding.

**Table 2: Total dose, fetal dose and outcome of pregnant patients undergoing radiotherapy**

H.B. Kal and H. Struikmans, Radiotherapy during pregnancy: fact and fiction, The Lancet Oncology 6(5), 328-333 (2005).

AAPM guidelines require the estimation and reduction of fetus dose  
 → In clinical setting it is important to perform experiments in phantoms and/or Monte Carlo simulations to estimate fetus dose



# Dosimetry in pregnancy radiotherapy





# Out-of-field doses during photon radiotherapy

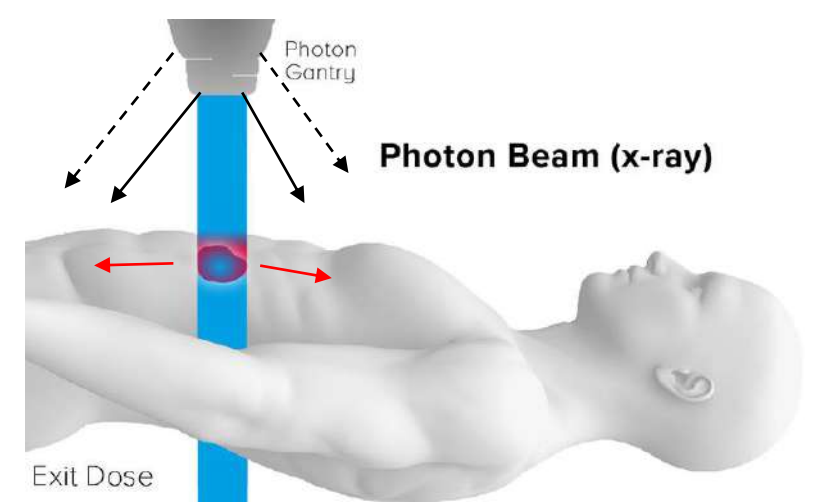
Source of out-of-field doses

- (1) photon leakage through the treatment head of the machine
- (2) radiation scattered from the collimators
- (3) radiation scattered within the patient from the treatment beams

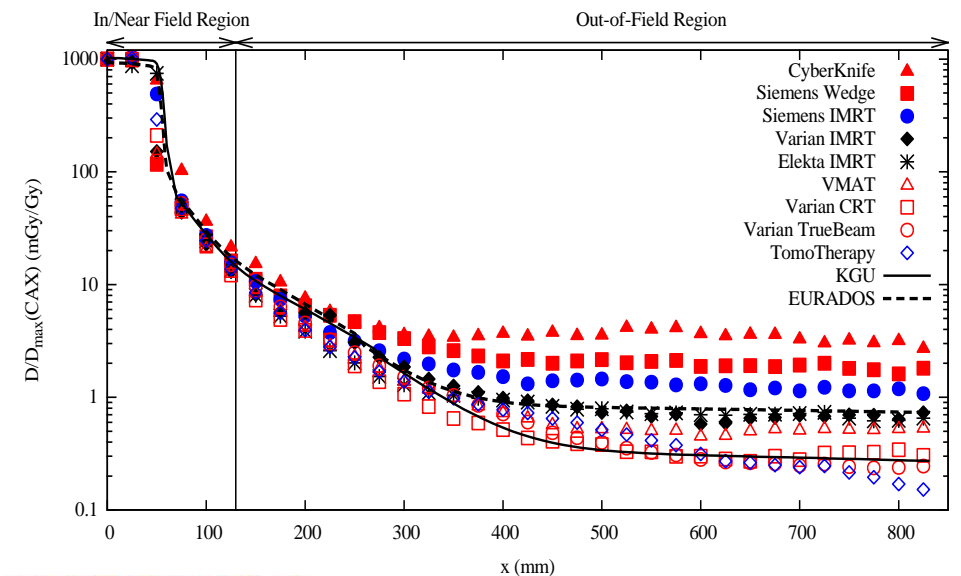
Out-of-field dose depends on

- Treatment device (Siemens, Varian, Elekta)
- Treatment technique
  - Conformal, IMRT, VMAT, Cyberknife

- > Head leakage
- > Head scatter
- > Patient scatter



Comparison of experimental WG9 EURADOS data to analytical model of different RT techniques and devices



# Phantom measurements for out-of-field dosimetry

## Water phantoms

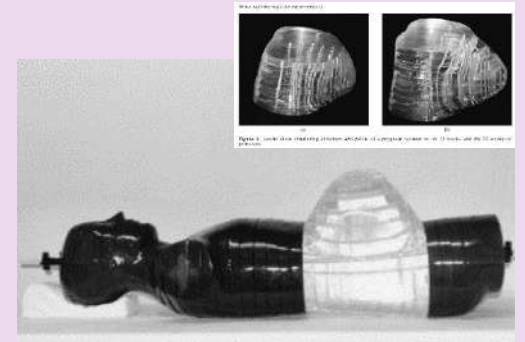


## Anthropomorphic

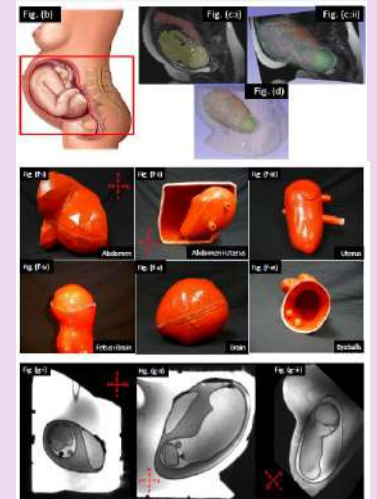


## Pregnant women

- No commercial phantom exists
- Water phantoms
  - No patient geometry and tissue composition
- Rando phantom
  - 1<sup>st</sup> stage of pregnancy (uterus dose)
- Rando plus PMMA/lucite slices
  - Belly of different sizes
  - Inserts for detectors
- 3D printing technology
  - Fetus organs can be modelled



LS Chitty 1994

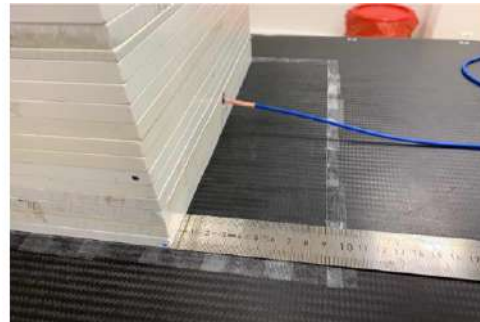
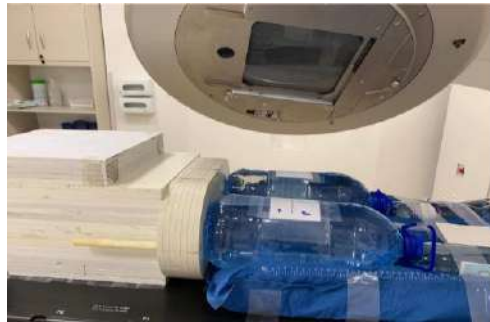
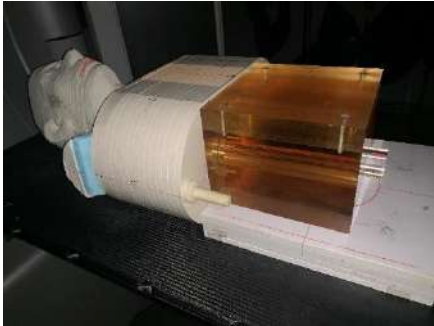


Group from USA (Boston, MA) designed and built MRI phantom that mimics critical organs (torso, uterus, placenta, fetal brain and body) and typical fetal motion in pregnancy at 36-weeks of gestational age

# Phantom measurements in clinics

## Fetal dose measurements

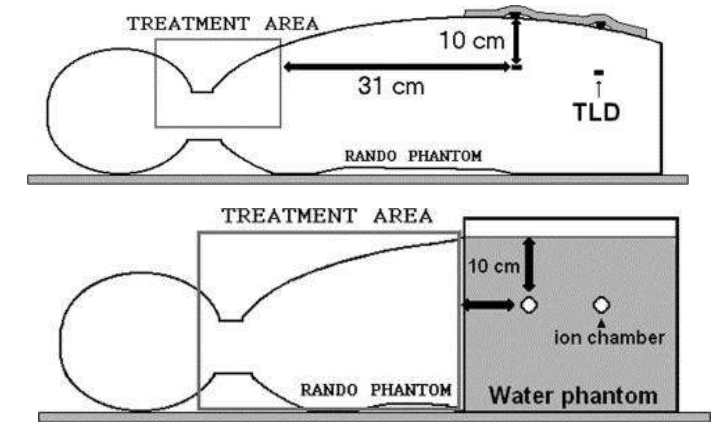
- Anthropomorphic phantom is used
  - Slabs of phantom
  - Water phantom added
- Combination of phantom pieces and water bottles
- TLDs, Ionization chambers are inserted and/or place on phantom



Provided by A. Kuchcińska., et al. NIO-PIB, Warsaw Poland



Z.E. Labby, et al. Rad Oncol Phys 2018



J.J. Nuyttens, et al. Cancer 2002

## Fetal dose optimization

- Beam parameters
- Positioning of patient
- Patient shielding
- Bladder filling

# Computational fetal dosimetry

- Patient imaging data are limited to the treatment area
  - Fetus is not scanned to avoid imaging dose to the fetus
- Make use of computational phantoms
  - Katja phantom – 24 weeks pregnancy (Helmholtz Zentrum Munich)
  - University of Florida family of anthropomorphic phantoms
    - 8, 10, 15, 25, 30 and 35w after conception



Figure 1. Katja and the fetus on the left hand side, on the right the primal model ICRP-AP. Clearly visible is the shifted colon. In the pelvis of ICRP-AP is the unchanged uterus

*J. Becker, et al. Pol J Med Phys Eng 2008*

## UF/NCI Phantom Library – Pregnant Females

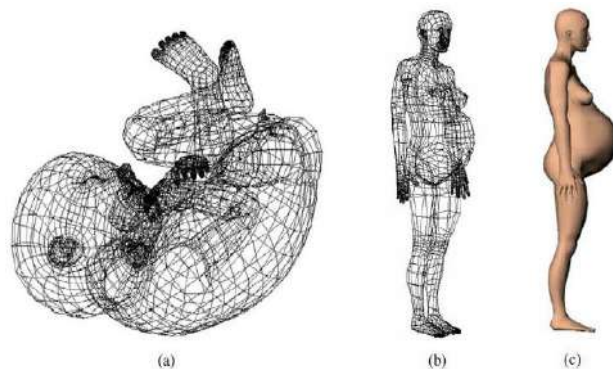
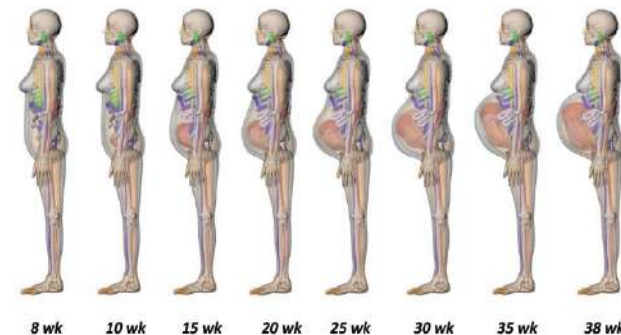
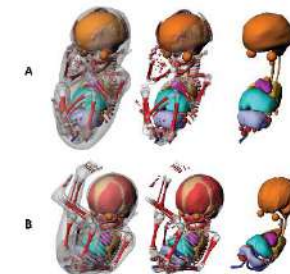


Figure 4. Models of the 9-month old fetus and the mother. (a) The adjusted skin surface model of the fetus model in mesh, (b) the adjusted skin model of the mother in mesh to accommodate for the fetus at 9-month gestation, (c) a surface rendering showing that the skin of the mother contains a 9-month old fetus.



The UF Family of hybrid phantoms of the pregnant female for computational radiation dosimetry  
 Phys. Med. Biol. 59 (2014) 4325–4343  
 Matthew B. Maynard<sup>1</sup>, Neria S. Long<sup>1</sup>, Nash S. Moawad<sup>2</sup>, Roger Y. Shulkin<sup>1</sup>, Amy M. Geyer<sup>1</sup>, Grant Fong<sup>1</sup> and Wesley E. Bolch<sup>1,3</sup>



The UF family of hybrid phantoms of the developing human fetus for computational radiation dosimetry  
 Phys. Med. Biol. 56 (2011) 4839–4879  
 Matthew B. Maynard<sup>1</sup>, John W. Geiser<sup>1</sup>, John P. Aris<sup>2</sup>, Roger Y. Shulkin<sup>3</sup> and Wesley Bolch<sup>1,2,3</sup>



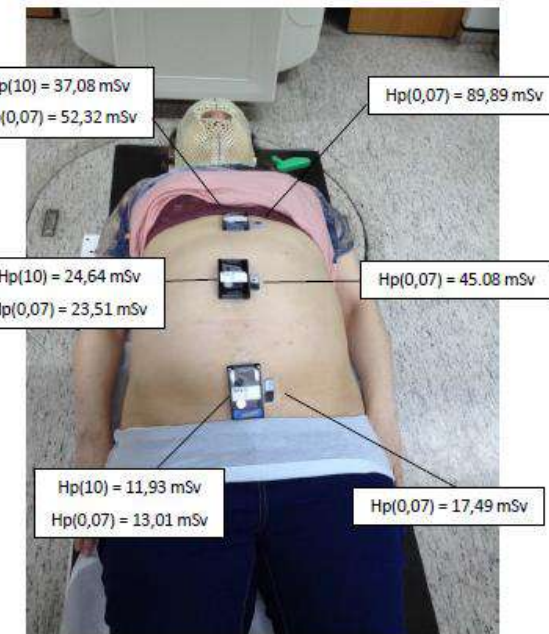
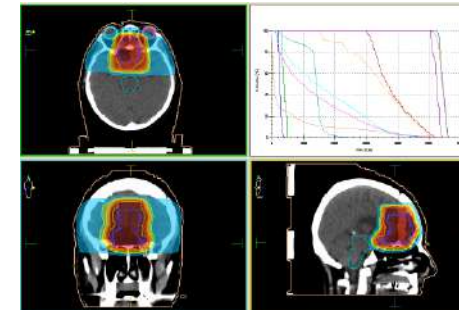
# In vivo patient dosimetry in clinics

Provided by A. Kuchcińska., et al. NIO-PIB

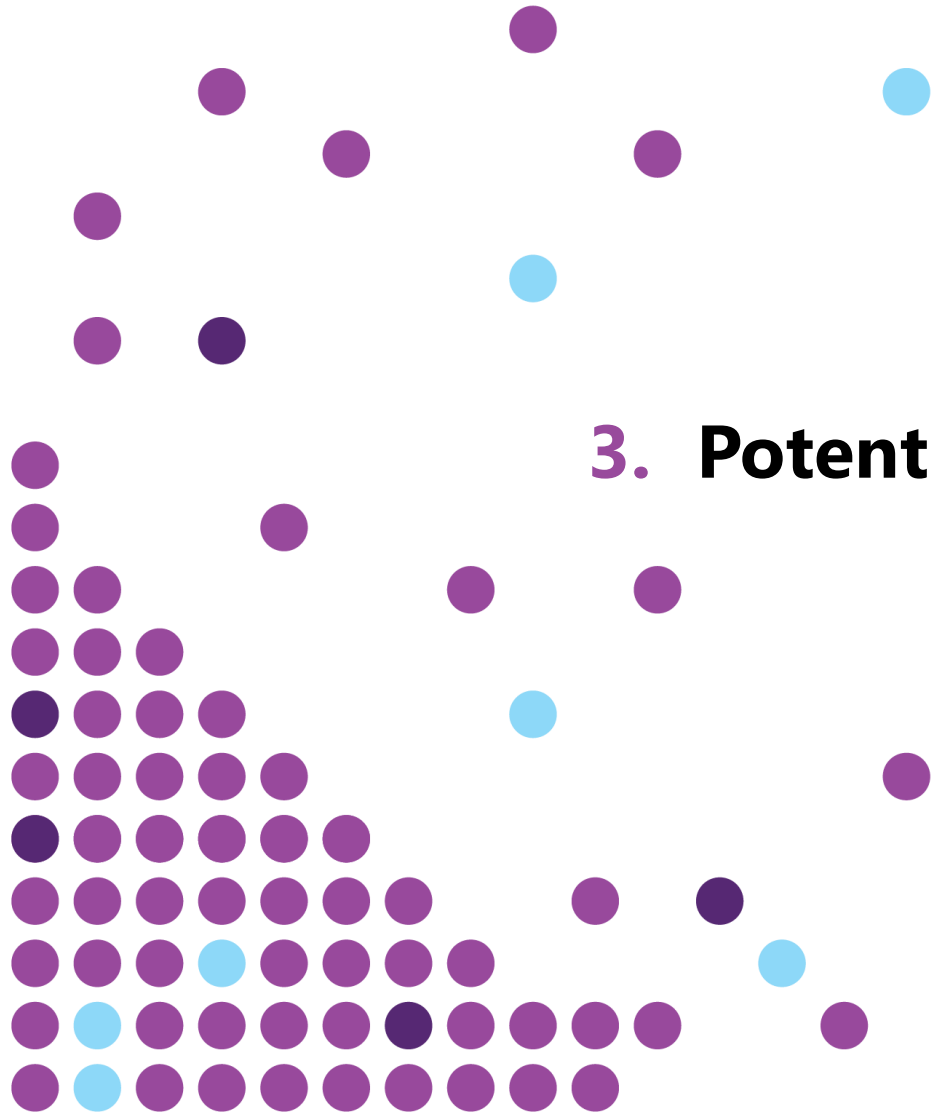
- Passive detectors on patient skin
- Assess skin dose and make use of phantom measurements for conversion to fetus dose



Sarcoma patient receiving RT during pregnancy



37y old pregnant women (21 weeks pregnant) with papilar meningioma (Grade III) is treated with 3D-CRT



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- 3. Potential benefit from advanced radiotherapy**
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# Potential benefit from advanced radiotherapy

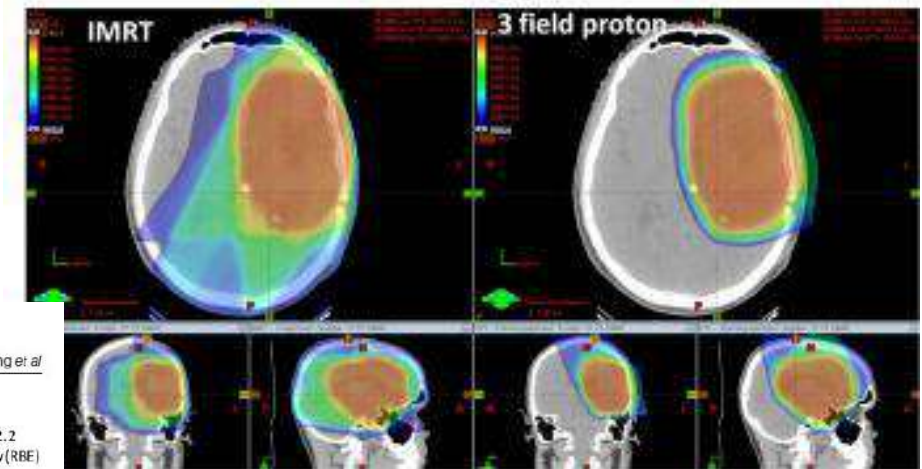
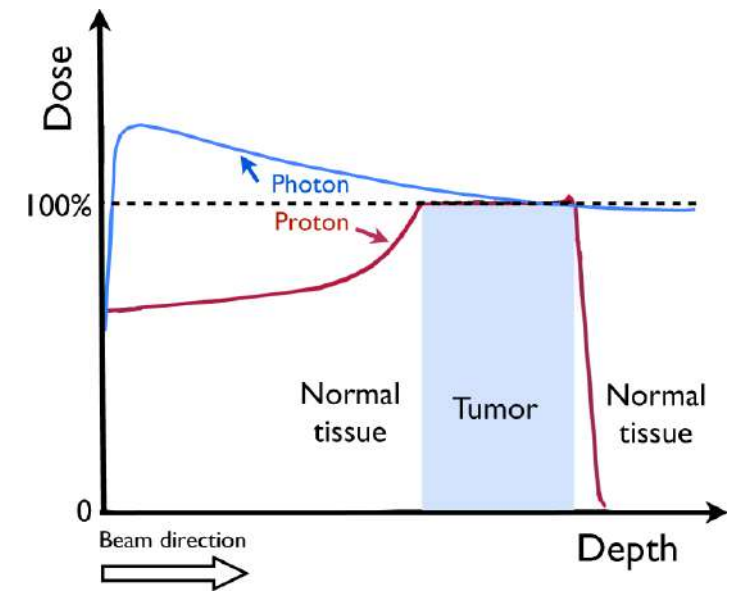




# Proton therapy

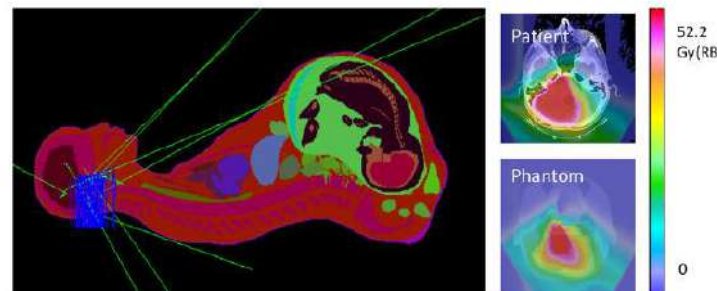
- Protons slow down as beam enters the target area and releases its energy at a tuneable depth in the tumour
  - Decreased entrance dose
  - No exit dose
- Few data exist on Proton Therapy during pregnancy
- Geng et al., 2015 calculated a 10-fold reduction in fetus dose during pregnancy
- Brain Pencil Beam Scanning versus 3D-CRT
  - PBS (1.5-2.5  $\mu\text{Sv}/\text{Gy}$ )
  - 3D-CRT (11-30  $\mu\text{Sv}/\text{Gy}$ )

Pregnant fetus dose data during PT are limited



Phys. Med. Biol. 61 (2016) 683

C Geng et al



# What are the dosimetry challenges?

- Protons interacting with beamline and patient creating secondary radiation
  - **Mixed field** radiation consisting of photons, protons, alphas and neutrons
    - Varying radiation qualities
    - Contribution to out-of-field dose depends on position out-of-field, patient orientation, beam parameters
  - Secondary **neutrons**
    - High-energy neutrons created by intra-nuclear cascades (up to maximum proton energy)
    - Fast neutrons evaporated by excited nuclei (few MeV)
    - Thermal neutrons by slowing down during collisions (0.25 eV)

Thermoluminescent detectors



- **Neutron detectors** for out-of-field dose assessment
  - Very specific detector material composition required
    - Thermal neutron detection based on  ${}^6\text{Li}(n,\alpha){}^3\text{H}$
    - Fast neutrons create recoil protons in Hydrogen rich materials → CR39 detectors
  - Need to be compact
    - Li6-enriched TLDs
    - CR39 detectors
    - Bubble detectors
  - Response is angular and energy dependent

Bubble detectors

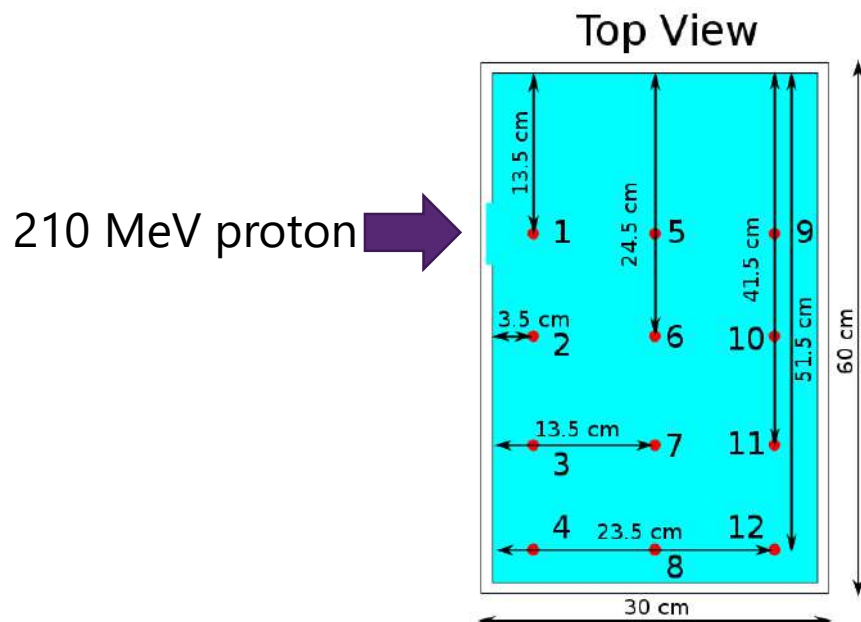


Track etch detectors

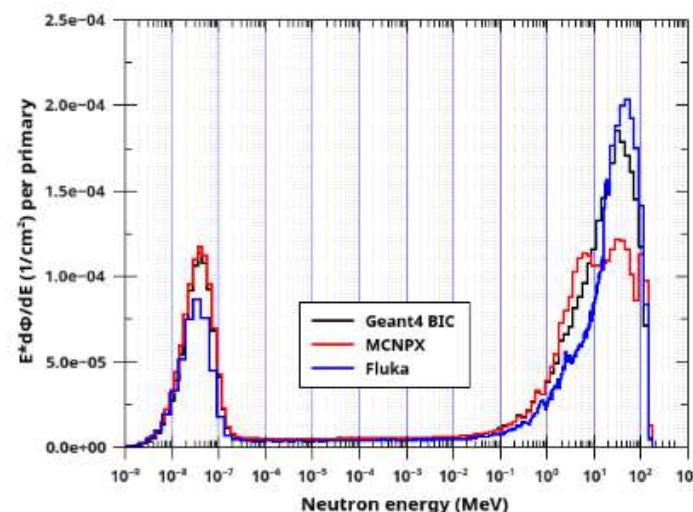


# What are the dosimetry challenges?

- **Monte Carlo** modeling of neutrons is challenging above 20 MeV
  - No cross section data exists and internuclear models are used
  - Strong dependency on the cross section libraries and models



Position 9



M De Saint-Hubert, , M. Klodowska, M. T. Romero-Expósito, Jad Farah, K. Tyminska, P. Olko and R. M. Harrison, S. Trinkl.  
 The Influence of Nuclear Models for the Prediction of Secondary Neutrons in Proton Therapy. Under preparation

→ Neutron dose calculations in proton therapy depend on the code and model used

# What dose quantity should be measured/simulated?

Case study – Heavy ion radiotherapy during pregnancy (Münter et al, 2010)

→ Active dosimeters

→ Neutron monitor (MAB NM 500X)

→ Gamma dose rate meter (TOL/F; Berthold)



H\*(10) is not providing you the right organ dose quantities

- **Organ dose equivalent (H<sub>T</sub>)**

- Secondary charged particles from neutrons

- Secondary photons

$$H_i = Q_i^n \cdot D_i^n + Q_i^\gamma \cdot D_i^\gamma,$$

Q(E) for neutron up to 20 MeV Siebert and Schumacher, et al., 1995 and NCR for neutrons up to 400 MeV

Q<sub>γ</sub>=1



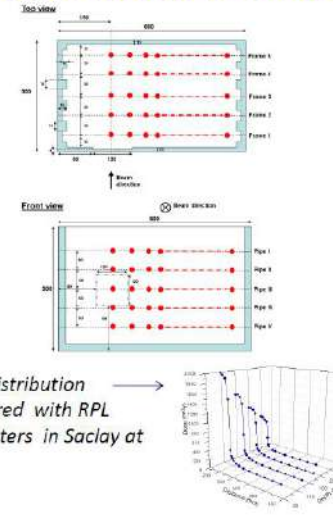
# What we know...

## EURADOS WG9

### Out-of-field proton dose

- 1-3 orders of magnitude lower than in photon therapy
- Further away from the target, neutron doses are dominant for the out-of-field doses
- Parameters influencing the dose
  - Use of range shifter
  - Proton energy
  - Field size
  - Patient position
    - Best set-up is perpendicular to the beam

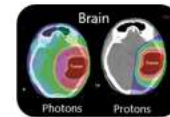
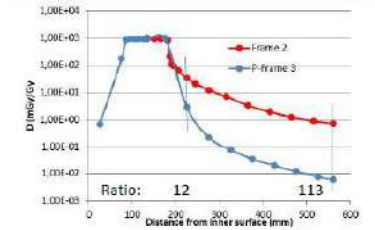
### WATER TANK MEASUREMENTS



Reference clinical LINAC Saturn 43, Saclay



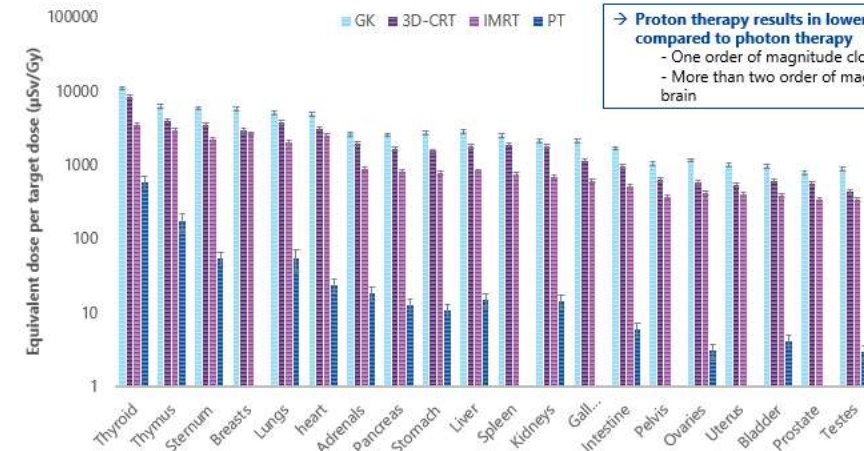
Proton Beam Scanning, IBA, Trento



### Proton therapy versus photon therapy



5-year old



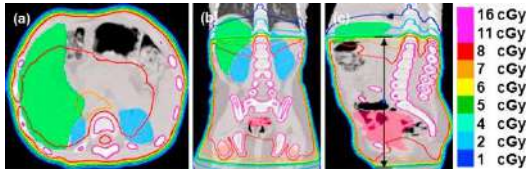
→ Proton therapy results in lower out of field doses compared to photon therapy

- One order of magnitude close to the brain
- More than two order of magnitude further away from the brain

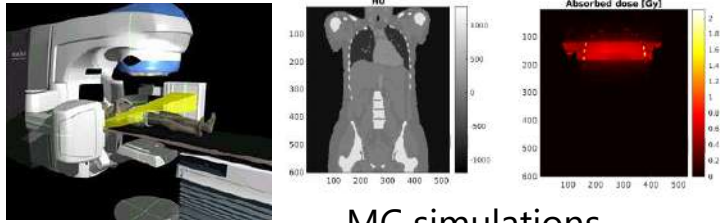
## EURADOS activities & plans



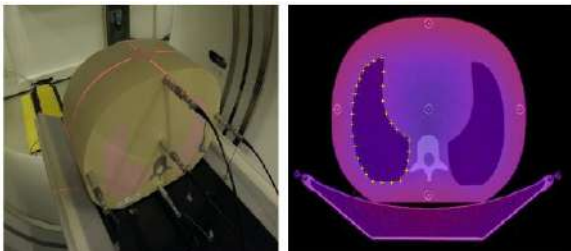
Total fetus dose including imaging dose



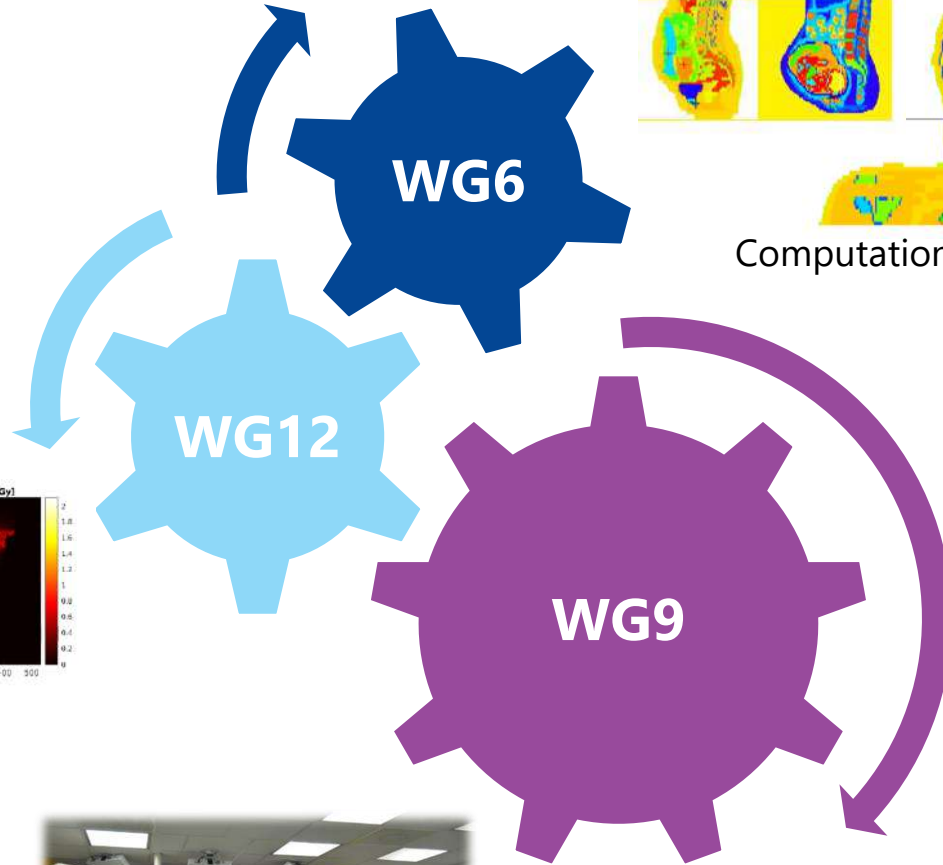
Imaging dose optimization



MC simulations



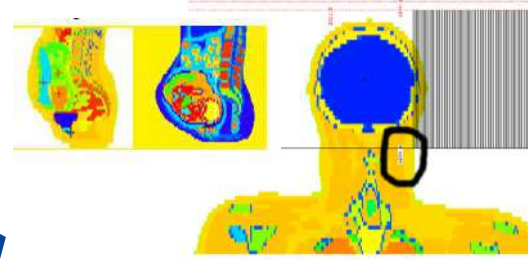
Measurements for imaging



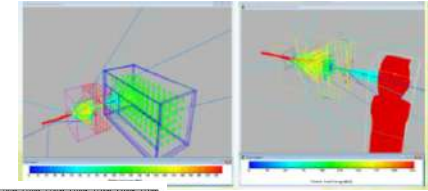
Measurement campaigns in RT clinics



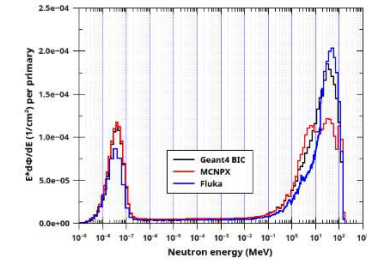
Monte Carlo simulation framework



Computational phantoms

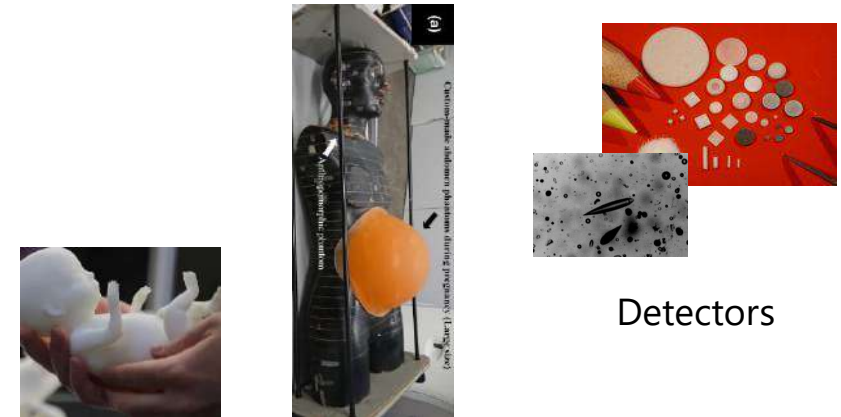


Beam modeling



MC modeling of neutrons

Phantom measurements of fetus doses in proton and photon radiotherapy



Detectors

Phantom development

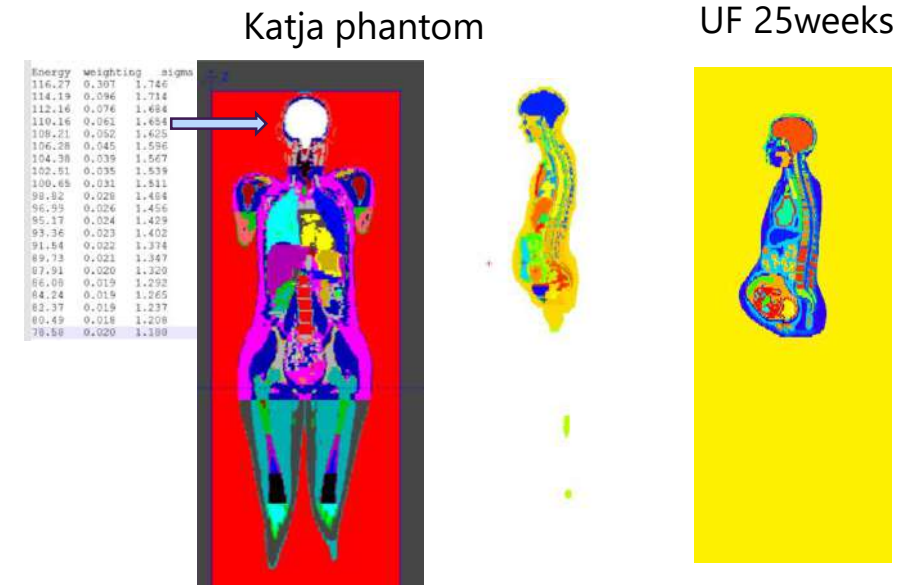


# Monte Carlo simulations of fetus dose

- Marijke De Saint-Hubert – SCK CEN (WG9)
- Hrvoje Brkic - MEFOS (WG9-6)
- Katarzyna Tyminska - NCBJ (WG6)



- Computational estimations of fetus dose during proton brain radiotherapy
  - MCNPx and MCNP6.2
    - Intercomparison of 2 MCNP versions
    - Impact of cross section data and nuclear models on fetus dose
  - Spread out bragg peak to treat brain tumor
    - 3cm collimated proton beam (range 10 modulation 5)
  - Katja (24 weeks) and UF 25 weeks phantom



Circular collimated proton beam of 3 cm diameter

# Monte Carlo simulations of fetus dose

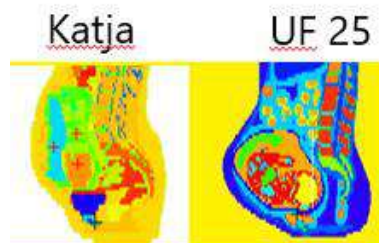
- Different default cross section libraries between MCNPx and MCNP6.2
  - Significant impact of data card on fetus dose
- Mix and match option using MX card we unified the cross section libraries and models between MCNPx and MCNP6.2
  - Very good agreement between codes and participants

- Fetus dose equivalent calculations

- Photon dose around 15%
- Fetus dose is dominated by neutrons
- Fetus dose = 20-40  $\mu\text{Sv}$
- 2-fold lower dose for UF25 compared to Katja

- slightly different stage
- different orientation

MCNP	Photon dose equivalent/ target dose	Neutron dose equivalent/ target dose	Total dose equivalent/ target dose	Total dose equivalent for 60 Gy target dose
Phantom	$\mu\text{Sv}/\text{Gy}$	$\mu\text{Sv}/\text{Gy}$	$\mu\text{Sv}/\text{Gy}$	$\mu\text{Sv}$
Katja 24wks	0.09	0.56	0.66	<b>39</b>
UF 25wks	0.06	0.28	0.33	<b>20</b>



H. Brkic, M. De Saint Hubert, K. Tyminska, L. Stolarczyk - **Comparison of the calculated fetus dose during proton therapy of pregnant patient using MCNPX and MCNP6.2.** In preparation for Rad Meas 2021.

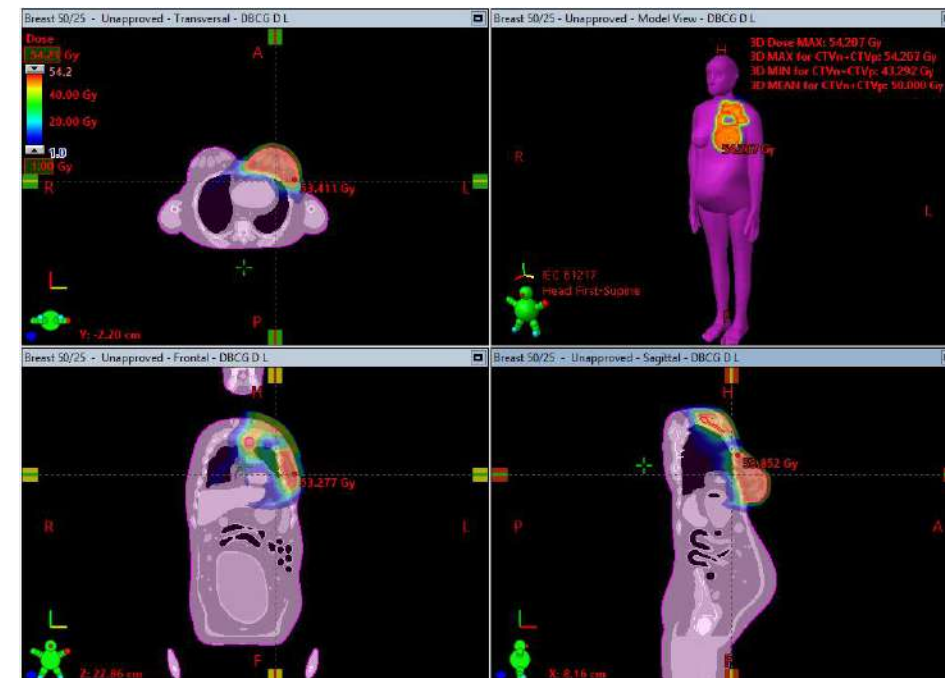
# What's next...



## Proton Breast plan on computational phantom

- DICOM-CT of UF 25 weeks phantom
- Danish Centre for Particle Therapy, Aarhus, Denmark
  - Linh My Hoang Thai
  - Maria Fuglsang Jensen
- Left sided breast + 6 lymph nodes
- 3 beams (10, 30, 50 degrees)
  - All using range shifters
- TOPAS wraps and extends the Geant4 Simulation Toolkit
  - DICOM-RT interface
  - Simulate the fetus dose
  - Comparison with MCNP
    - Modeling of neutron dose
    - Impact of simplified beam parameters

Danish Centre for Particle Therapy, Aarhus, Denmark



Original paper

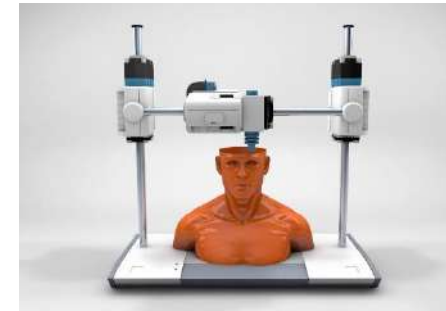
DICOM-RT Ion interface to utilize MC simulations in routine clinical workflow for proton pencil beam radiotherapy

Jungwook Shin<sup>a,b,\*</sup>, Hanne M. Kooy<sup>a,b</sup>, Harald Paganetti<sup>a,b</sup>, Benjamin Clasié<sup>a,b</sup>

<sup>a</sup>Department of Radiation Oncology, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114, USA  
<sup>b</sup>Harvard Medical School, Boston, MA, USA

# Phantom measurements of fetus doses in proton and photon radiotherapy

- Phantom development
  - BfS - Sebastian Trinkl
    - 3D printer for pregnant phantom and fetus printing
    - Currently testing printing approaches and materials
- Measurements photon and proton therapy
  - Interest from WG9 participants
  - Passive (TLD, RPLD, Track edge, BD..) and active detectors (timepix, CMOS, ...)
  - Out-of-field dose estimations in proton therapy mixed field
    - Miguel Ángel Caballero-Pacheco (UAB) on 'Methodology on out-of-field doses in proton radiotherapy' – Eurados grant 2021



3D phantom printing



# Total fetus dose including imaging dose

## WG 12 - Dosimetry for medical imaging

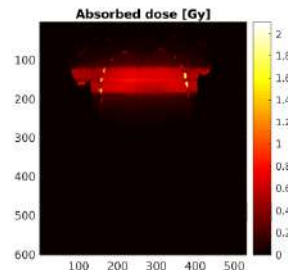
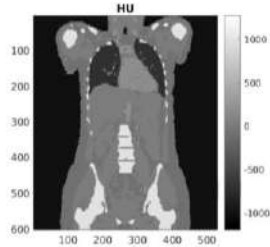
### Sub-group 2 – patient dosimetry

#### Project on total dose in radiotherapy (WG6/9/12) - Coordinated by Teemu Siiskonen



#### Imaging doses in radiotherapy

- Assess the situation in Europe (imaging protocols/parameters, estimate patient doses)
- Develop methods for easy estimation of personalised doses from imaging (simulations and empirical methods)
- Collaborate with other organisations to provide good practice guides and recommendations (IAEA, ICRP, EFOMP)



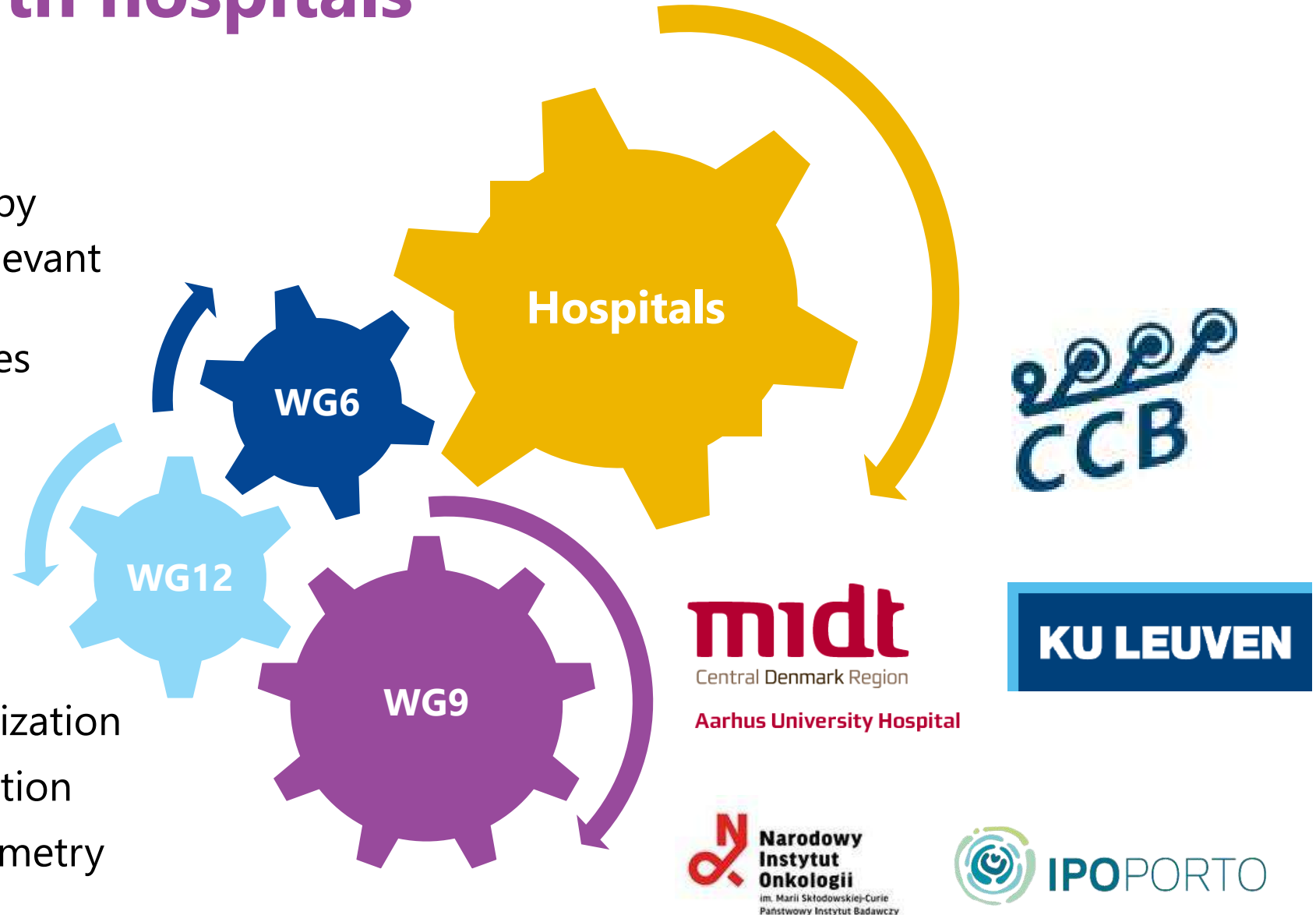
#### Task 4: Dosimetry in pregnancy related to medical exposure (Dario Faj)

- Review literature and available cases from own practice and experience
- Questionnaire on available algorithms
- Case study/intercomparison plus analysis of uncertainty
- Phantom measurements/MC simulations

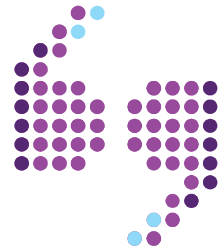
# Collaboration with hospitals

## Clinical experience

- Fetus dose from radiotherapy
  - Different and clinically relevant indications
  - Different pregnancy stages
- Execute clinical plans
  - Computational
  - Physical phantoms
  - Host measurements
- Treatment parameter optimization
- Include imaging + optimization
- Towards individualized dosimetry approach...







Thank you for your attention



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