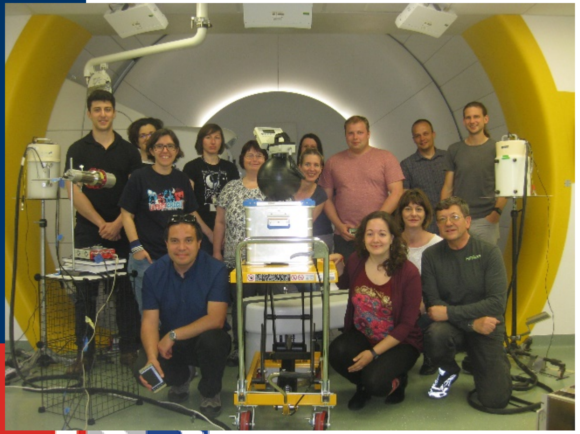
# *Out-of-field doses during pediatric radiotherapy*

*Željka Knežević*
Ruđer Bošković Institue, Zagreb, Croatia
On behalf of WG9



Why out of field doses?

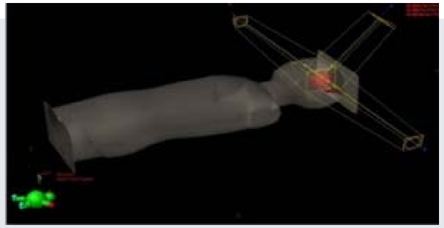
Why paediatric patients?

Why brain tumor simulations?

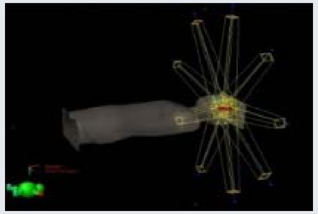
Why proton therapy?

- Unwanted doses, deposited distantly from the target volume (**out-of-field doses**), may lead to an increasing probability of late effects of RT including the generation of **secondary cancers**
- **Paediatric patients** are of particular concern due to their possible longer life expectancy and increased organ radiosensitivities compared to adult patients
- Clinical simulations of **brain tumours** RT (brain tumours are second most common tumours in children
- **Proton beam therapy** has clear advantages in terms of short- and long-term complications which is especially important when tumours are located next to critical organs and while treating cancer in paediatric patients
- Photon RT vs Proton RT

# Measurements of secondray radiation in photon RT

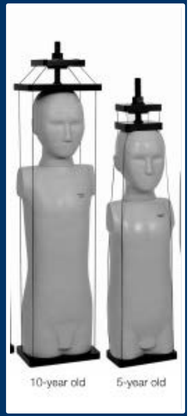


3D-CRT (Varian)



IMRT (Varian)

## Brain tumor simulations




**3D-CRT** (Krakow 2013)
Varian Clinac 2300
3 non-coplanar beams (6MV), 336MU
Dynamic and mechanical wedge

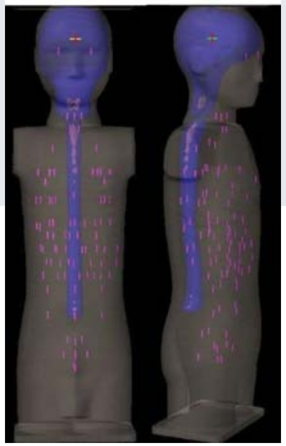
**IMRT** (Krakow 2013)
Varian Clinac 2300
9 coplanar beams (6MV) 443MU

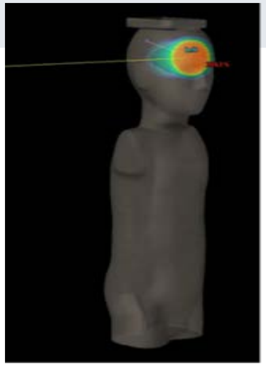
**GK** (Zagreb 2014)
Leksell GK, Co-60 sources

## Craniospinal irradiations (CSI)

**3D-CRT** (Osijek 2020)
**Brain irr.** : 2 lateral fields (90°, 270°), 6 MV
**Spinal cord irr.** 1 posteroanterior (PA) field (180°), 10 MV

**VMAT** (Osijek 2020)
Two arcs (full rotation), 6 MV





# 2. Measurements of  secondray radiation in proton RT

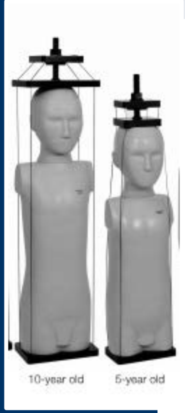
- Brain tumor simulations
- Craniospinal irradiations
- shallowly located tumour simulation

Proton Beam Scanning (PBS) , IBA gantry  (IBA, Proteus 235)  at the Bronowice Cyclotron Centre  (IFJ PAN, Krakow, Poland)

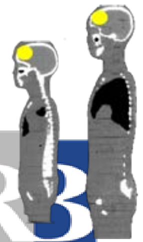
IMPT

range shifter vs 3D printed compensator

PT (IBA, Proteus C-325)

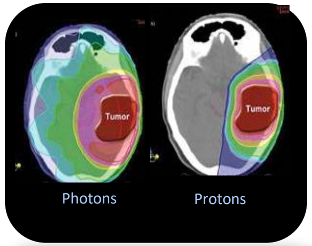



≈middle of the target



# *Out-of-field doses in pediatric craniospinal irradiations with 3D-CRT, VMAT, and scanning proton radiotherapy*

## *Selected results*

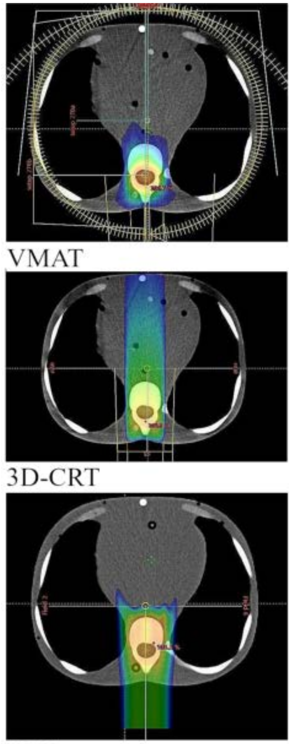



*M. Majer et. al. Out-of-field doses in pediatric craniospinal irradiations with 3D-CRT, VMAT and scanning proton radiotherapy - a phantom study, Med. Phys. 49 (2022), 4; 2672-2683*

# Out-of-field doses in CSI irradiations with 3D-CRT, VMAT, and scanning proton RT

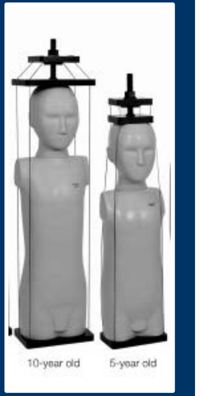
- CSI has greatly increased survival rates for patients with a diagnosis of medulloblastoma
- CSI requires irradiation of a large target volume covering the entire brain and spinal cord

includes exposure of a large volume of healthy tissue to unwanted doses, - strong concern about the complications of the treatment, especially for the children




## Aim

To evaluate and compare out-of-field doses in pediatric CSI treatment using conventional and advanced **photon RT** and **proton RT**



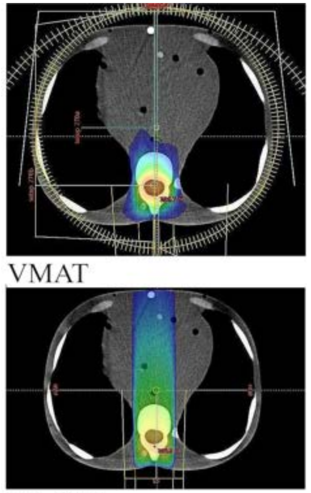

| RT technique | Photon radiotherapy | | Proton radiotherapy |
|---|---|---|---|
| | 3D-CRT | VMAT | PBS |
| RT center | Osijek University Hospital (OUH), Croatia | | Cyclotron Centre Bronowice (CCB), Poland |
| Accelerator | Varian Clinac iX (Varian Medical Systems, Palo Alto, CA) | | Ion Beam Applications S.A. (IBA) proton therapy system – Proteus C 235 (Ion Beam Applications SA) |
| TPS | Eclipse, version 15.6.06 (Varian Medical Systems, Palo Alto, CA) | | Eclipse, version 13.6 (Varian Medical Systems, Palo Alto, CA) |
| Dose algorithm | Analytical anisotropic algorithm (AAA) | Acuros algorithm | Proton Convolution Superposition algorithm |
| Brain irradiation | Two lateral fields (90°,270°), 6 MV | Two arcs (full rotation), 6 MV | Two lateral fields (90°, 270°), with a range shifter, 73.7–180.9 MeV[a] |
| Spinal cord irradiation | One posteroanterior (PA) field (180°), 10 MV | | Three PA fields (180°), with a range shifter, 78.4–142.2 MeV[a] |

| Dosimetry system | Used for: | |
|---|---|---|
| RPL (GD-352M) | Photon dose measurements, $D$(mGy) |  |
| Nuclear Track detectors (PADCs) | Neutron measurements $H_n$ (mSv), |  |

# Craniospinal irradiations- photon techniques (VMAT and 3D CRT)

## Comparison of the mean organ dose/target dose (photon doses) with TPS

Larger nonuniformity in dose is generally shown for larger organs spreading from dorsal to ventral parts of the body and therefore experiencing larger dose gradients.




## VMAT

- the mean doses to all organs of interest were under 50% $D_T$ (<500mGy/Gy)
- TPS underestimated the doses

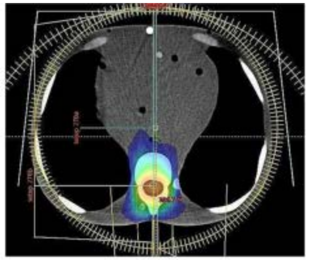
| Organ | VMAT $\bar{D}/D_T$ (mGy/Gy) | VMAT $\bar{D}_{TPS}/D_T$ (mGy/Gy) |
|---|---|---|
| Prostate | 8 | 5 |
| Bladder | 11 (30%) | 9 (40%) |
| Intestine | 117 (57%) | 109 (58%) |
| Gall Bladder | 174 (4%) | 166 (4%) |
| Stomach | 144 (29%) | 129 (29%) |
| Liver | 166 (37%) | 156 (36%) |
| Lungs | 147 (34%) | 140 (33%) |
| Breasts | 49 (6%) | 45 (1%) |
| Oesophagus | 451 (34%) | 420 (39%) |
| Thyroid | 164 (20%) | 142 (14%) |
| Eyes | 280 (10%) | 238 (3%) |
| Average | 156 | 142 |

*M. Majer et. al. Out-of-field doses in pediatric craniospinal irradiations with 3D-CRT, VMAT and scanning proton radiotherapy - a phantom study, Med. Phys. 49 (2022), 4; 2672-2683*

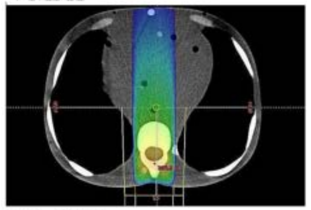
# Craniospinal irradiations- photon techniques (VMAT and 3D CRT)

## Comparison of the mean organ dose/target dose (photon doses) with TPS

Larger nonuniformity in dose is generally shown for larger organs spreading from dorsal to ventral parts of the body and therefore experiencing larger dose gradients.



VMAT



3D-CRT

| Organ | VMAT $\bar{D}/D_T$ (mGy/Gy) | VMAT $\bar{D}_{TPS}/D_T$ (mGy/Gy) | 3D-CRT $\bar{D}/D_T$ (mGy/Gy) | 3D-CRT $\bar{D}_{TPS}/D_T$ (mGy/Gy) |
|---|---|---|---|---|
| Prostate | 8 | 5 | 8 | 11 |
| Bladder | 11 (30%) | 9 (40%) | 19 (60%) | 25 (43%) |
| Intestine | 117 (57%) | 109 (58%) | 273 (128%) | 262 (127%) |
| Gall Bladder | 174 (4%) | 166 (4%) | 507 (75%) | 407 (82%) |
| Stomach | 144 (29%) | 129 (29%) | 134 (166%) | 152 (144%) |
| Liver | 166 (37%) | 156 (36%) | 234 (129%) | 214 (127%) |
| Lungs | 147 (34%) | 140 (33%) | 31 (40%) | 41 (46%) |
| Breasts | 49 (6%) | 45 (1%) | 31 (15%) | 37 (3%) |
| Oesophagus | 451 (34%) | 420 (39%) | 747 (42%) | 768 (18%) |
| Thyroid | 164 (20%) | 142 (14%) | 592 (32%) | 632 (13%) |
| Eyes | 280 (10%) | 238 (3%) | 9 (2%) | 105 (5%) |
| Average | 156 | 142 | 242 | 241 |

### VMAT

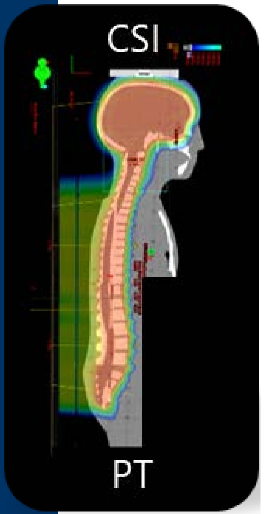
- the mean doses to all organs of interest were under 50% $D_T$ (<500mGy/Gy)
- TPS underestimated the doses

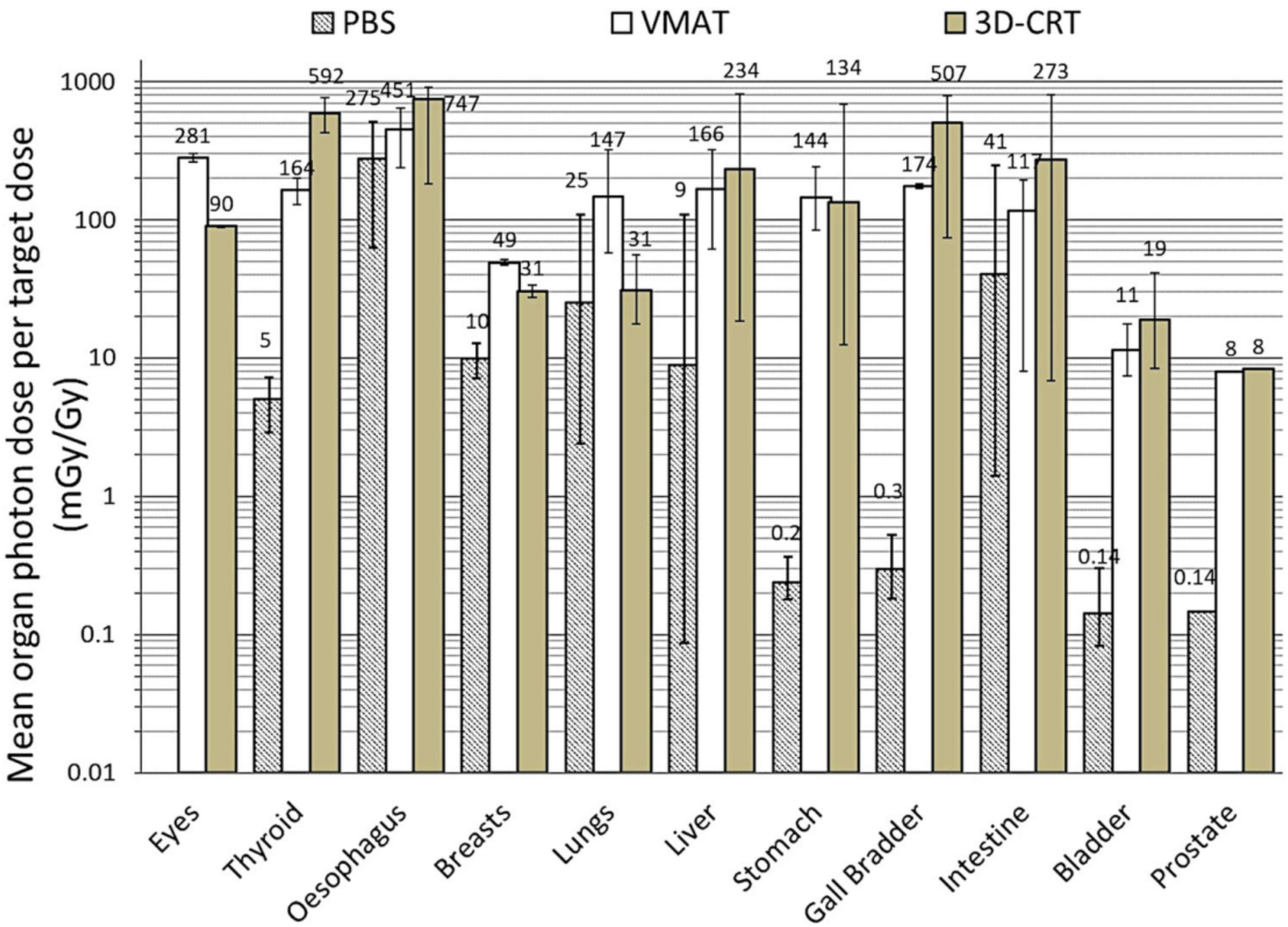
### 3D-CRT

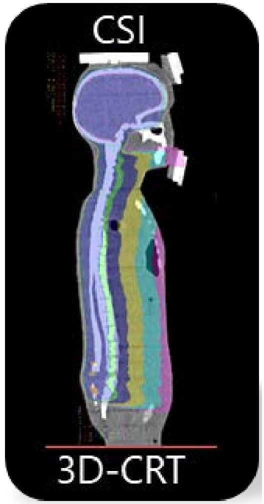
- dose to thyroid, oesophagus, and gall bladder exceed 50% $D_T$
- TPS in general overestimates the mean organ doses
- The highest overestimation is for organs at the largest distances

M. Majer et. al. Out-of-field doses in pediatric craniospinal irradiations with 3D-CRT, VMAT and scanning proton radiotherapy - a phantom study, Med. Phys. 49 (2022), 4; 2672-2683

## Comparison of the mean organ dose/target dose (photon doses)



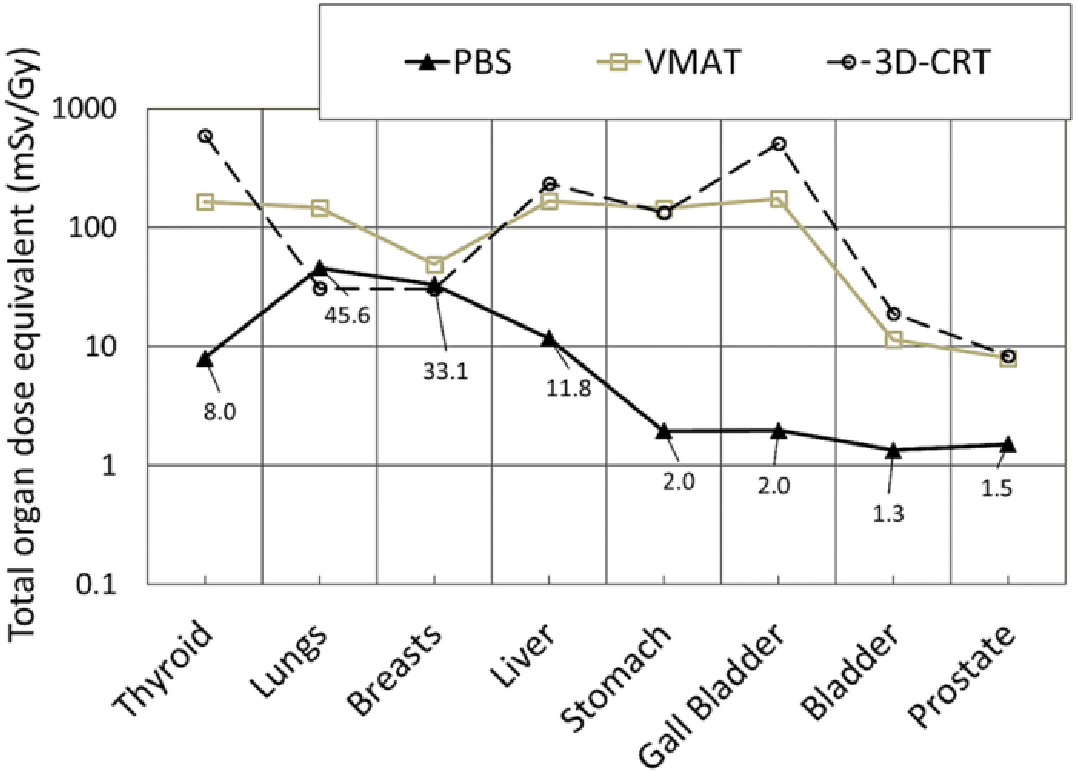

## Proton CSI

- For all organs, much lower mean dose compared to photon techniques (from several times for lungs and breasts, and up to 3 orders of magnitude for stomach and gall bladder).

## Comparison of the Total organ dose equivavlent (mSv/Gy)

3D-CRT better sparing for lungs, eyes, and breasts
VMAT is a better choice for most of the out-of-field organs and especially for thyroid

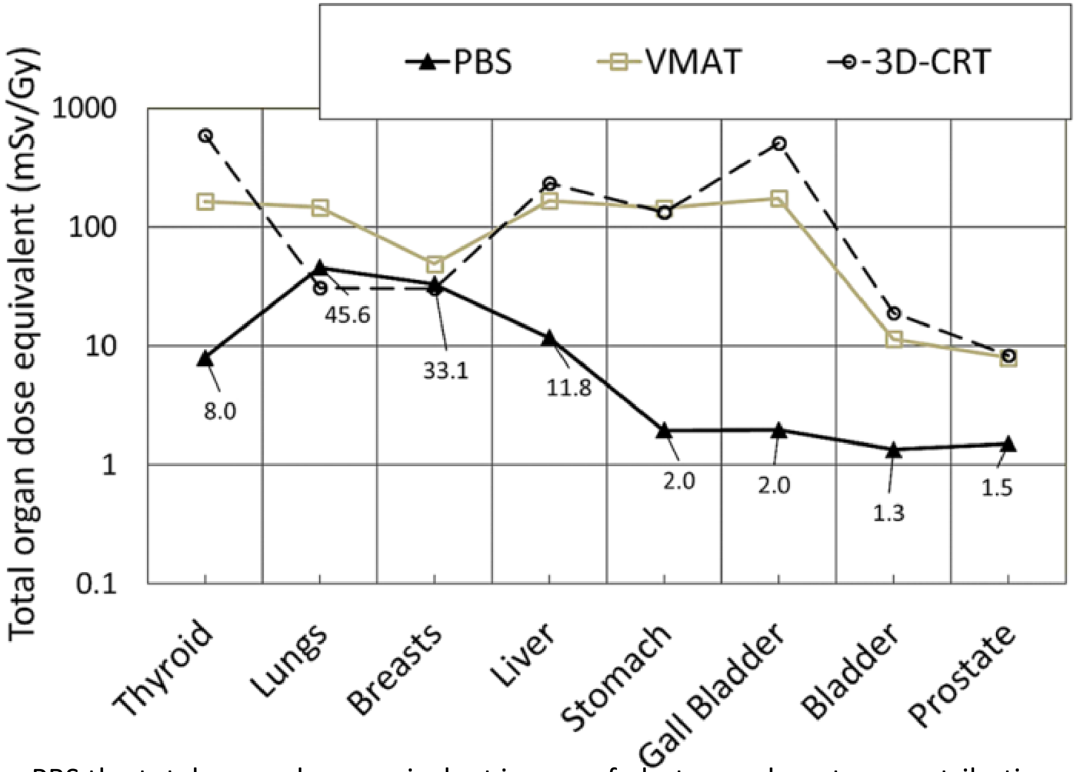
More conformal treatment and up to 2 orders of magnitude lower out-of-field doses measured in this study confirmed the advantage of PBS proton RT over photon RT




*for PBS the total organ dose equivalent is sum of photon and neutron contributions

## Comparison of the Total organ dose equivavlent (mSv/Gy)

VMAT is a better choice for most of the out-of-field organs and especially for thyroid 3D-CRT better sparing for lungs, eyes, and breasts



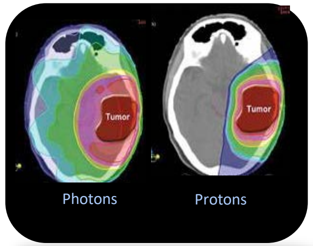

*for PBS the total organ dose equivalent is sum of photon and neutron contributions

More conformal treatment and up to 2 orders of magnitude lower out-of-field doses measured in this study confirmed the advantage of PBS proton RT over photon RT

An important criterion for the selection of a RT technique is the dose to eyes, thyroid, lungs, and breasts due to second cancer risk but also the risk of eye disease, hypothyroidism, and pneumonia.
especially important to reduce doses (and risk) for young girls due to the strong sex and age dependence of the risk coefficients.

According to measured photon and neutron doses in this study, PBS is a strongly recommended RT technique.

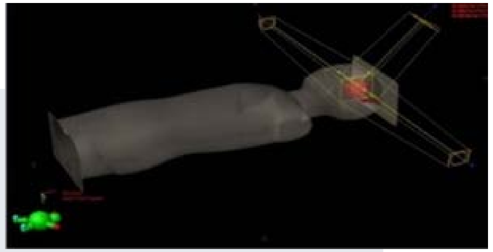

# *Out-of-field doses in proton spot scanning RT versus photon therapy*




M. Majer et al. *Out-of-field dose measurements for 3D-CRT and IMRT of a paediatric brain tumor*. Radiat. Prot. Dosim. 176 (2017), 3; 331-340
M. De Saint-Hubert, M. Majer et al. *Out-of-field doses in children treated for large arteriovenous malformations using hypofractionated GK and IMRT*, Radiat. Prot. Dosim. 181 (2018)
Ž. Knežević et al. *Out-of-Field Doses Produced by a Proton Scanning Beam Inside Pediatric Anthropomorphic Phantoms and Their Comparison With Different Photon Modalities*. Front. in Oncol. 12 (2022); 904563, 14

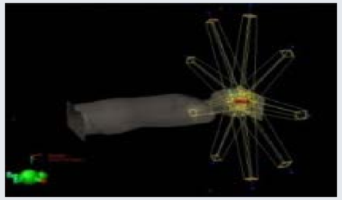
# Measurement campaigns

**3D-CRT** (Krakow 2013)
Varian Clinac 2300
3 non-coplanar beams (6MV), 336MU
Dynamic and mechanical wedge



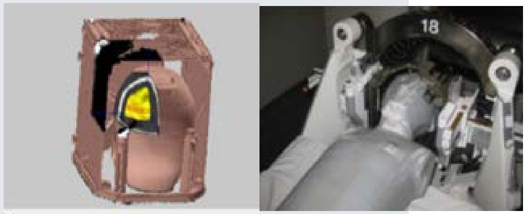
3D-CRT (Varian)

**IMRT** (Krakow 2013)
Varian Clinac 2300
9 coplanar beams (6MV) 443MU



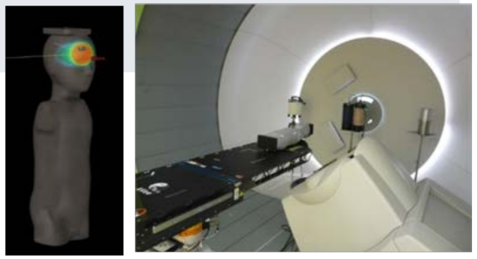
IMRT (Varian)

**GK** (Zagreb 2014)
Leksell GK, Co-60 sources

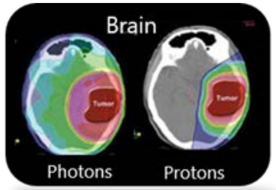


Leksell Gamma Knife

**Proton therapy** (Krakow 2014)
Proteus 235 (IBA), CCB in Krakow
Spot scanning (70.5-144.6 MeV)
**Modality:** (IMPT) coplanar beams (140° and 270°)

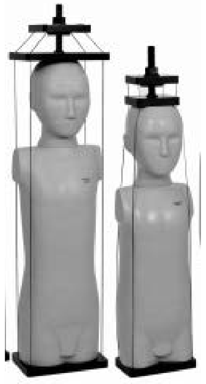


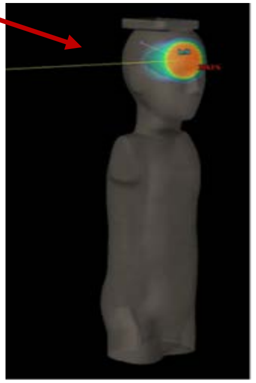
**Proton therapy** (IBA, Proteus C-235)




## Brain tumor simulations

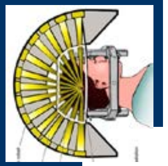
**Target:** spherical brain tumor with 6cm diameter, volume 65 $cm^3$ with the isocentre in the head of the phantom



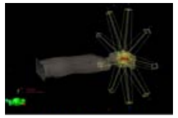



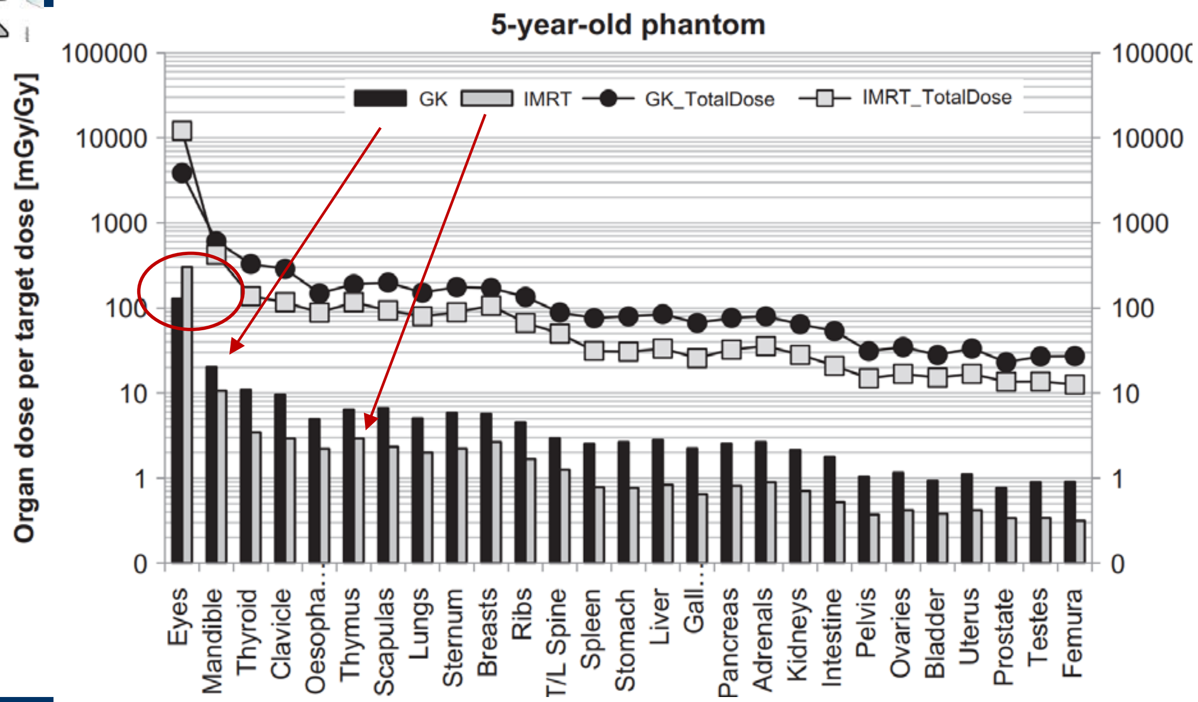
**Detectors:** TLDs, RPLs, track-etched and BD were inserted in phantom on different organ positions

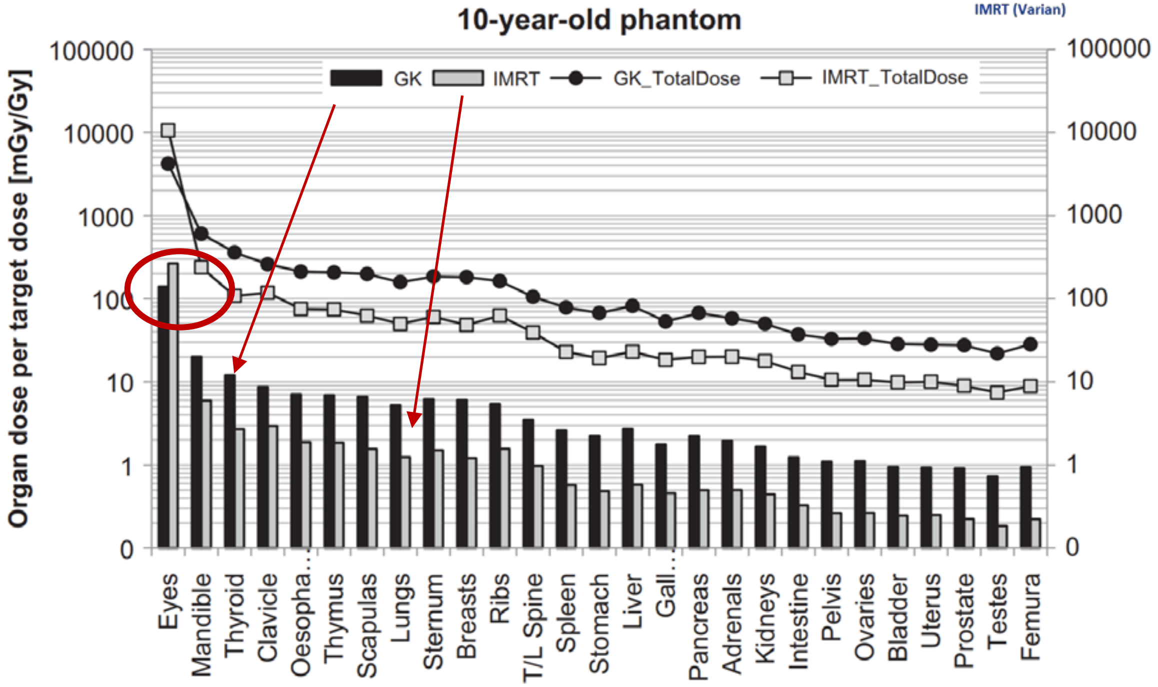
# Out-of-field doses photon RT



*Organ dose per target dose [mGy/Gy] **GK and IMRT**



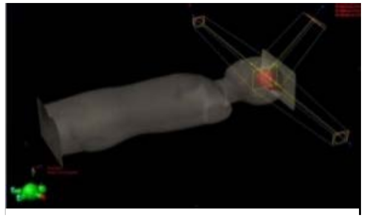

Figures taken from*

- The study showed that for children with large size brain AVMs treated with hypofractionated GK radiosurgery the eyes were better spared with GK
- higher other out-of-field organs doses with GK compared to the highly conformal IMRT technique
- for more distant organs doses up to a factor of 2.8 and 4 times larger for GK compared to IMRT in 5y and 10y phantoms

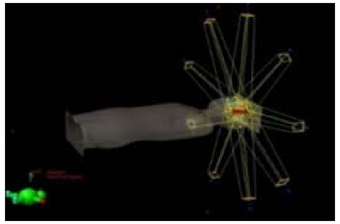
*M. De Saint-Hubert,M. Majer et. al. Out-of-field doses in children treated for large arteriovenous malformations using hypofractionated gamma knife radiosurgery and intensity-modulated radiation therapy Radiat. Prot. Dosim., 181 (2018), 2; 100-110

# Out-of-field doses **photon** RT

*Comparison of measured doses for **3D-CRT and IMRT** as a function of distance from the isocentre



**3D-CRT** (Varian)



**IMRT (Varian)**

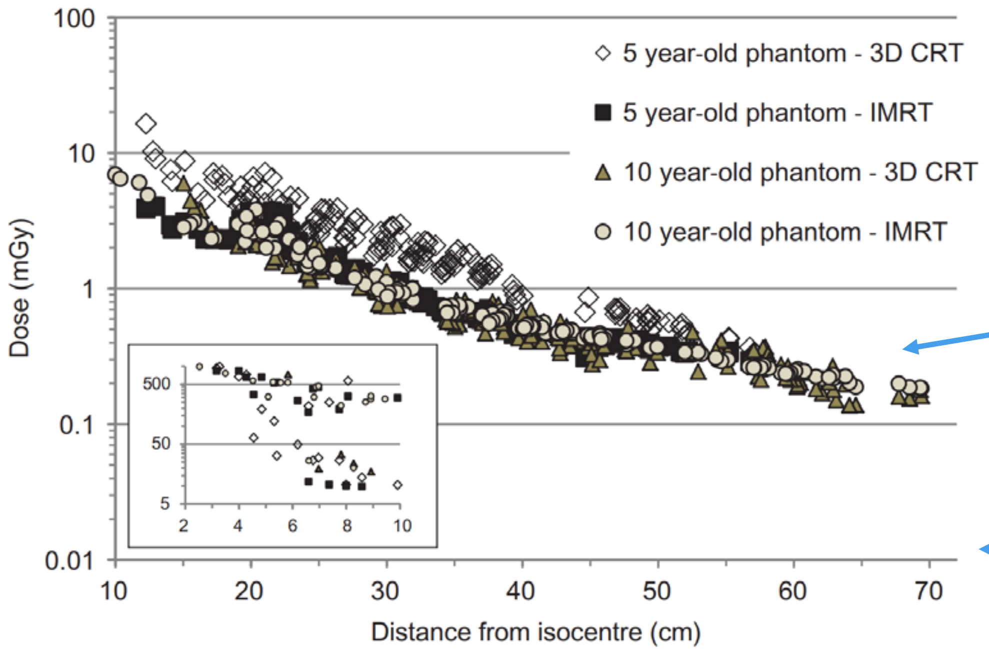



Figure taken from*

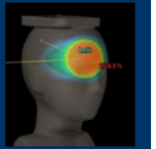
Measured doses

TPS<0.01

- The results showed, higher organ doses for the 5y than for the 10y phantom
- average 1.6 and 3.0 times **higher doses for the 5y** than for the 10y phantom for IMRT and 3D-CRT
- Comparison of measured doses and doses calculated by the TPS showed that the **TPS underestimated** out-of-field doses both for IMRT and 3D CRT.

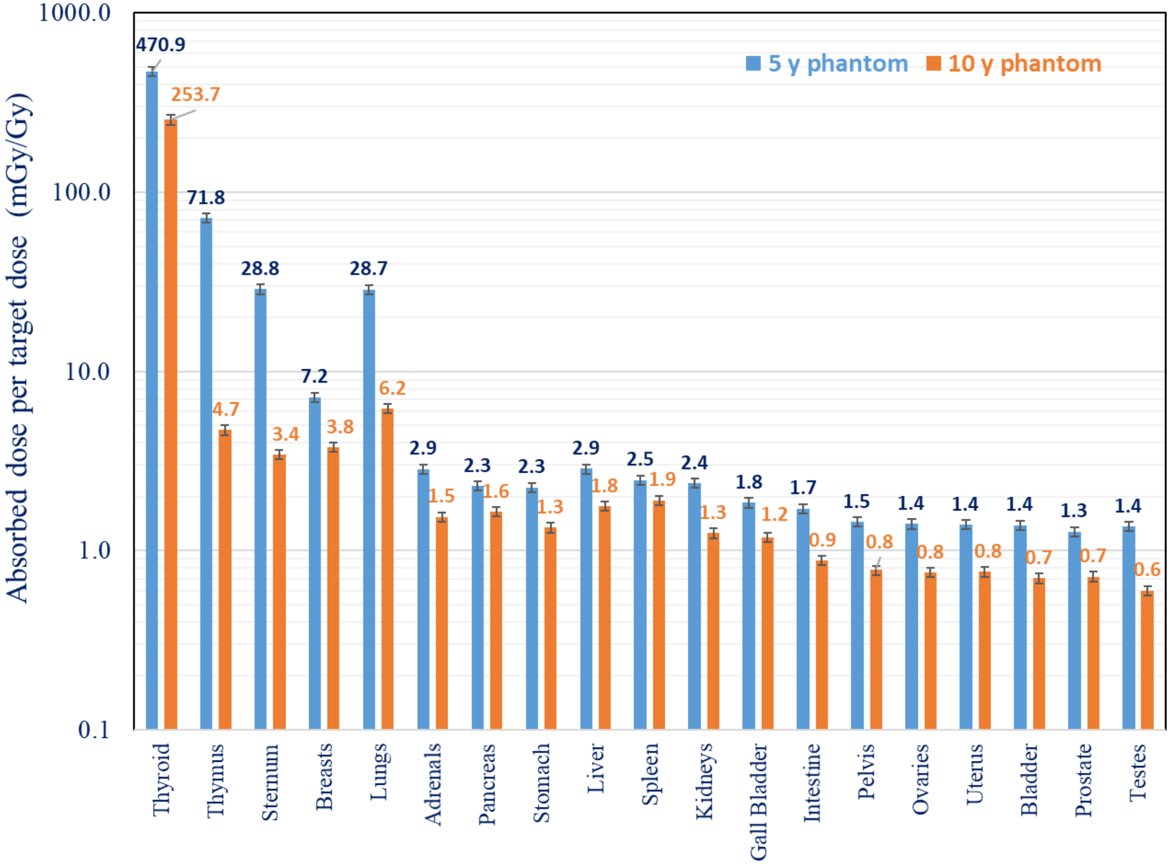
**M. Majer et. al. Out-of-field dose measurements for 3D conformal and intensity modulated radiotherapy of a paediatric brain tumour Radiat. Prot. Dosim., 176 (2017), 3; 331-340*

# Out-of-field doses in **proton** RT





## Comparison of *non-neutron organ doses for 5 y and 10 y phantom



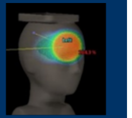

*non-neutron dose is used to express the fact that RPL detectors register not only gamma-rays, but also to a limited extent neutrons and some charged particles

Secondary non-neutron organ doses are **higher for 5 y phantom** compared to 10 y phantom

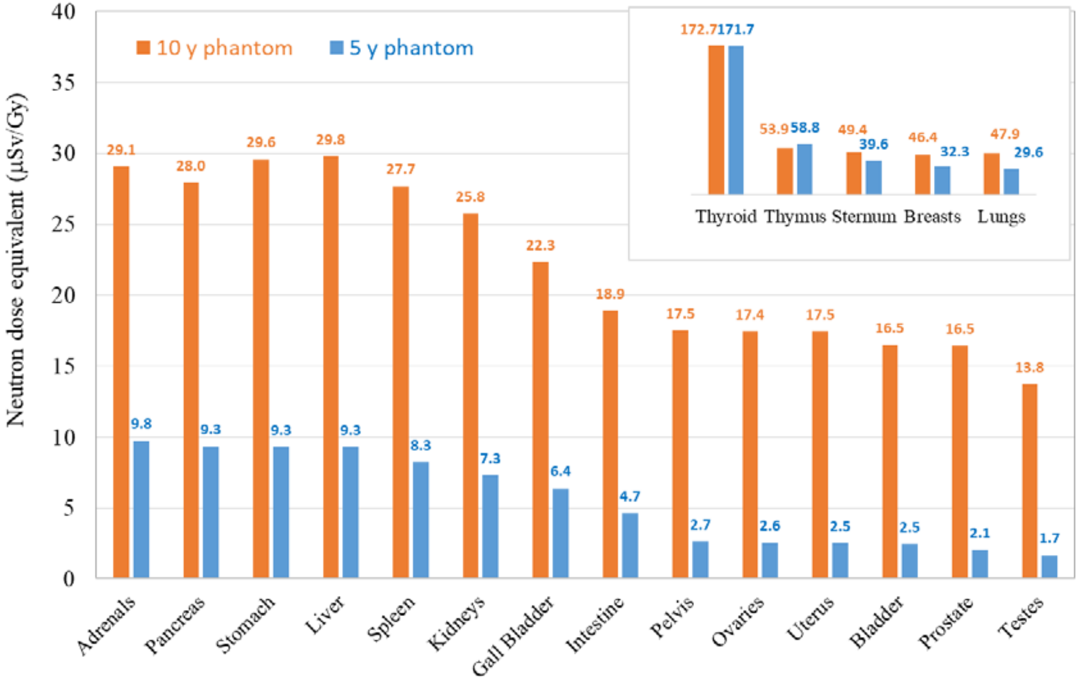
Smaller distance from healthy organs to irradiated target

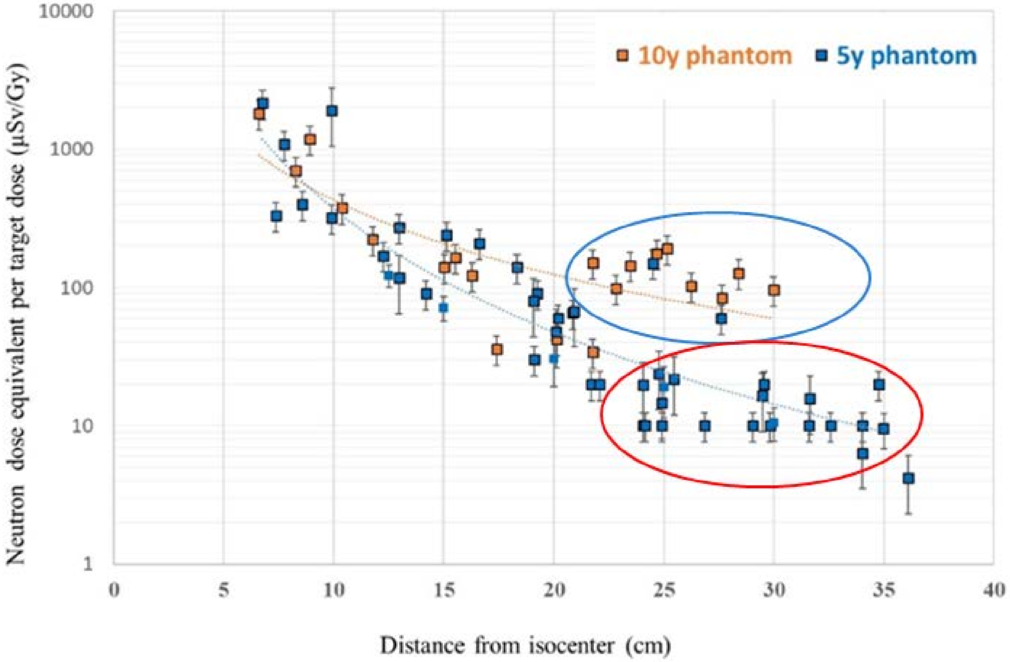
## Non neutron doses

- 5y ranged from **0.47 mGy/Gy** (13 cm) to **1.5 µGy/Gy** (50 cm)
- 10-y ranged from **0.25 mG/Gy** (15 cm) to **0.6 µGy/Gy** (70 cm)




## Comparison of neutron dose equivalent for 5 y and 10 y phantom

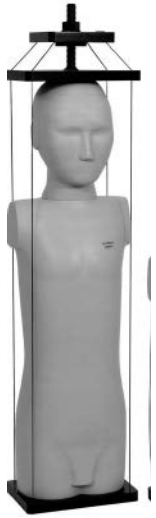



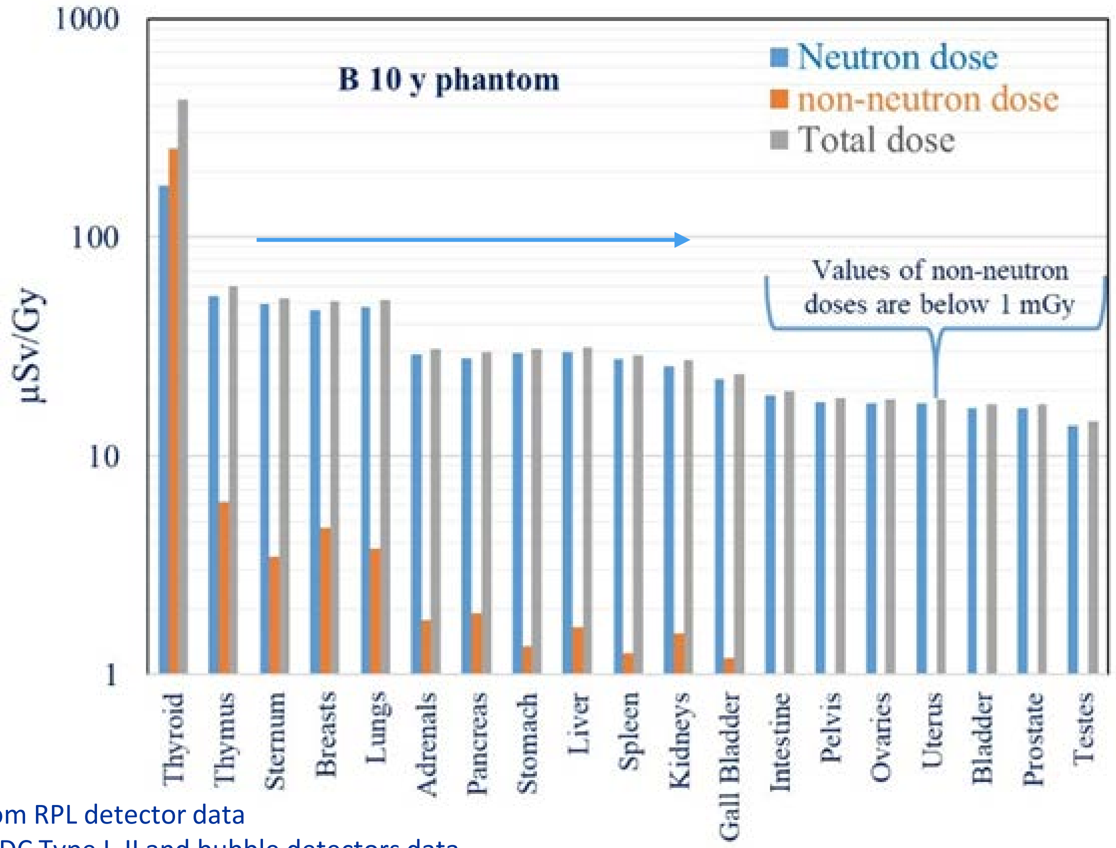




- The neutron dose equivalent, range from **1mSv/Gy** close to the field edge to **0.01 mSv/Gy at ≈30 cm** from the isocenter for 5y phantom
- Compared to 5y results show slightly **higher neutron doses** in 10y between 20 and 30 cm from the isocenter by factor of 2 and on average by factor of 4

# Out-of-field doses in proton RT

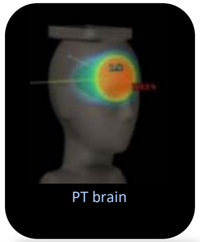
## Comparison of neutron, non-neutron and total doses


10-year old

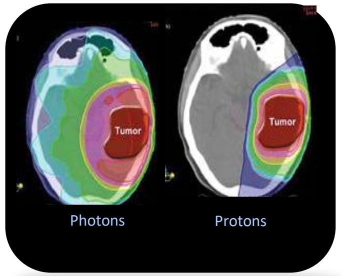



*Non-neutron doses caclulated from RPL detector data
*Neutron doses calulated from PADC Type I, II and bubble detectors data

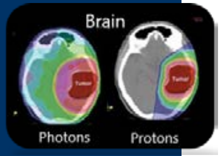
- Neutron dose are lower (factor of 3) than non-neutron doses close to the target while the secondary neutron dose becomes larger than non-neutron dose further away from the target
- In PT mean out-of-field total doses including neutron and non-neutron range: from **0.6 mSv/Gy (5y)** and **0.4 mSv/Gy (10y)** in thyroid to **<0.01 mSv/Gy** (both phantoms) in intestines, ovaries, bladder and testes



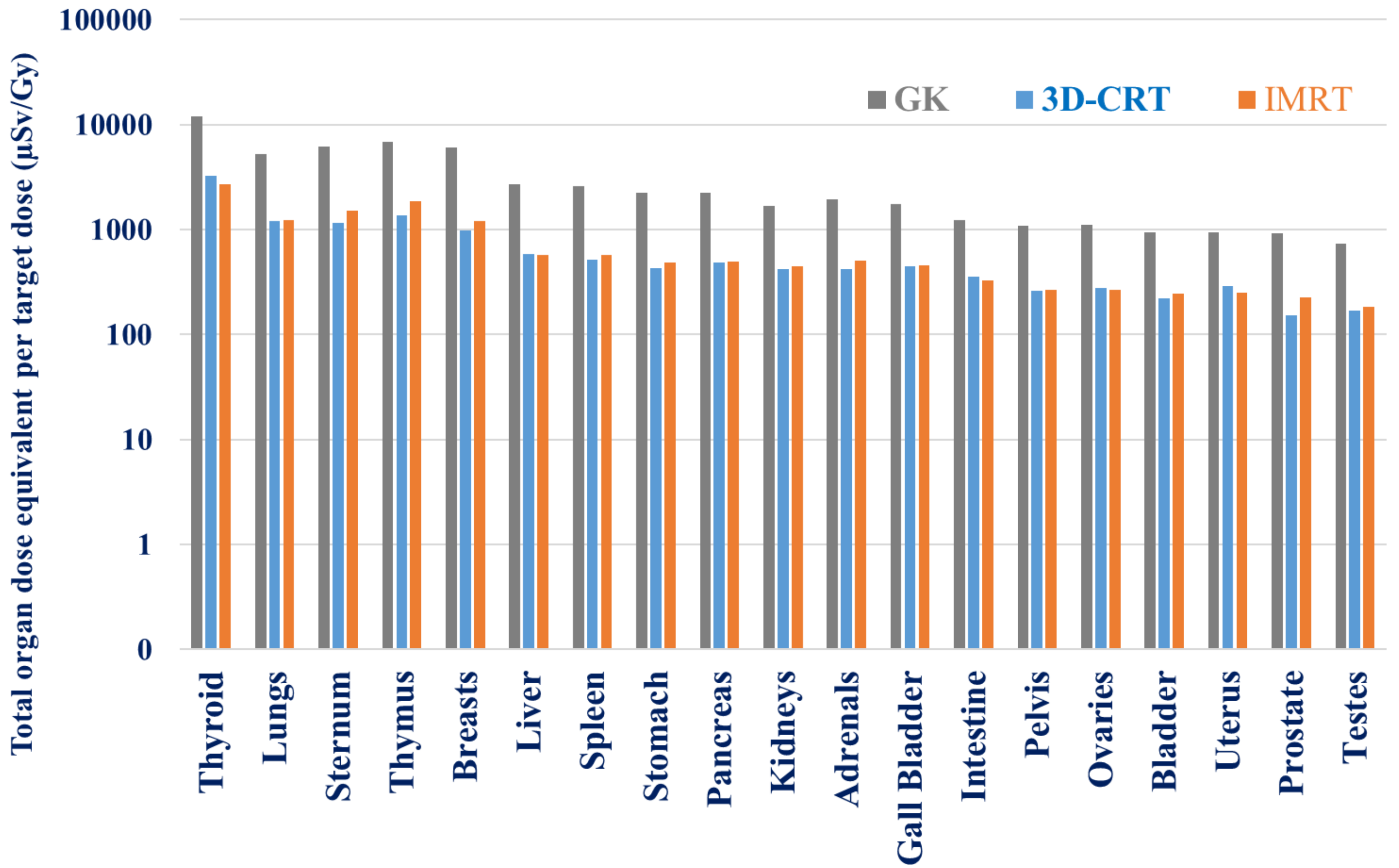

## *Comparison of measured secondary doses in IMPT with different photon therapy modalities*



# Proton therapy versus photon therapy (10y phantom)

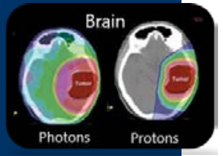




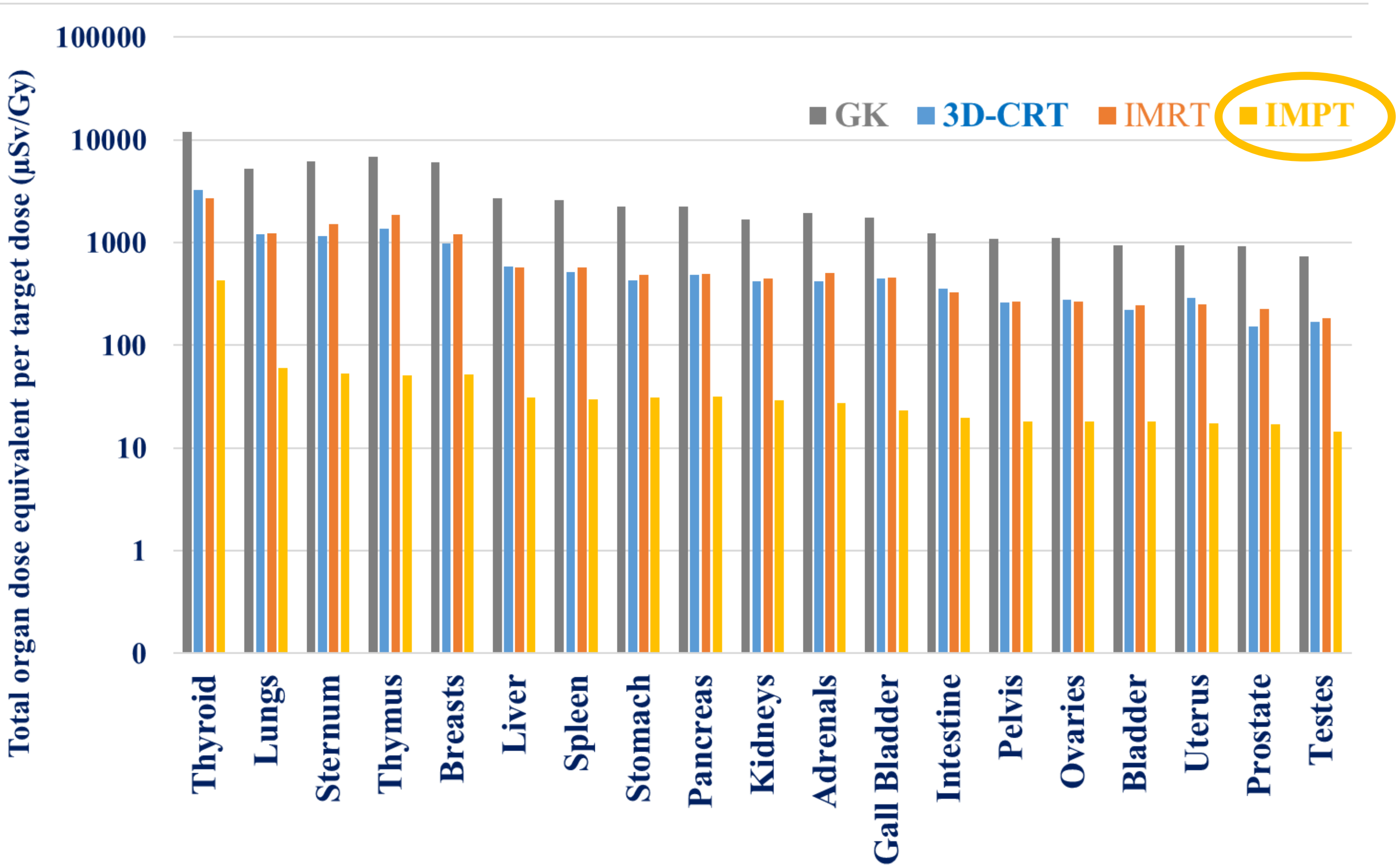



Ž. Knežević et al. Front Oncol 2022. Out-of-Field Doses Produced by a Proton Scanning Beam Inside Pediatric Anthropomorphic Phantoms and Their Comparison With Different Photon Modalities.

# Proton therapy versus photon therapy (10y phantom)







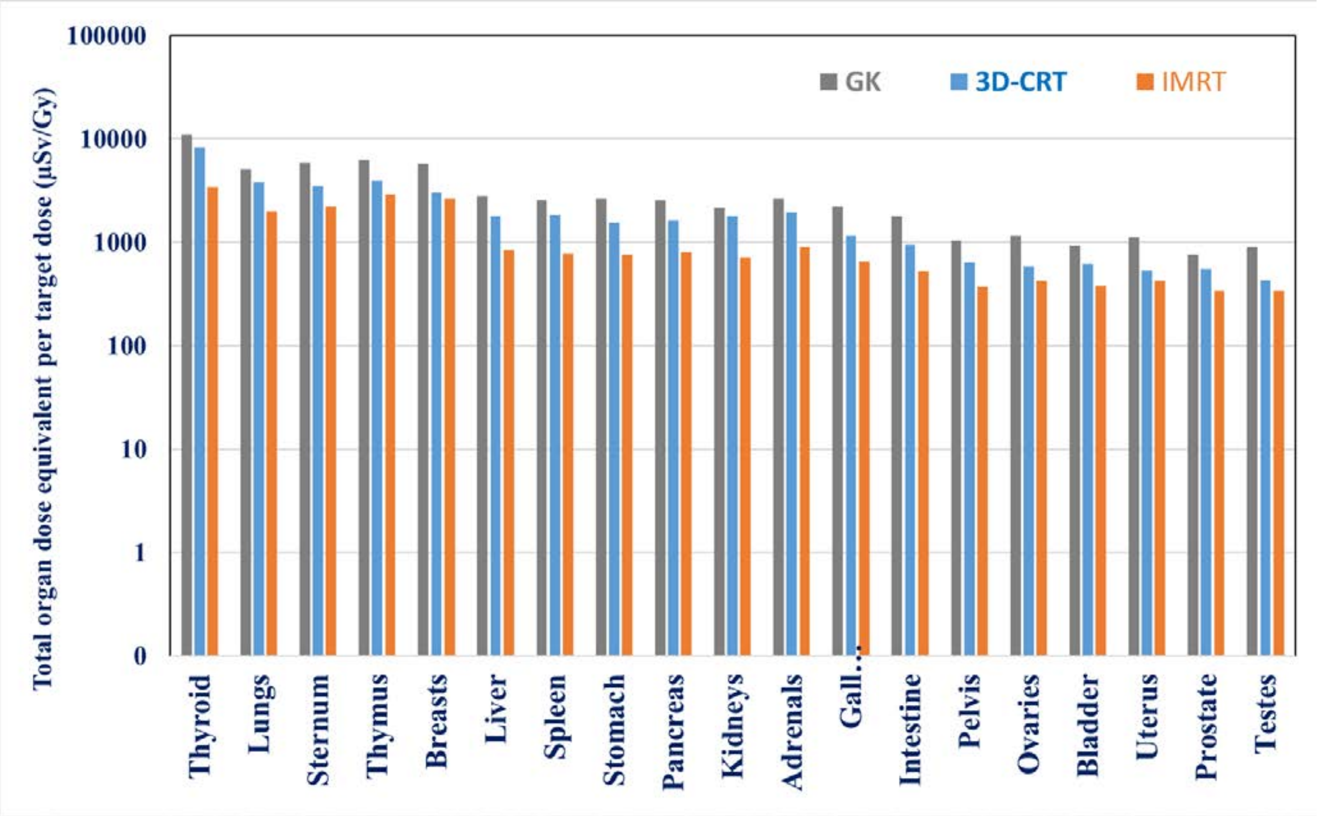

*for PBS the total organ dose equivalent is sum of photon and neutron contributions
*for photon techniques total out-of-field dose is considered to be out-of-field photon dose

**→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

*Ž. Knežević et al. Front Oncol 2022. Out-of-Field Doses Produced by a Proton Scanning Beam Inside Pediatric Anthropomorphic Phantoms and Their Comparison With Different Photon Modalities.*

# Proton therapy versus photon therapy (5y phantom)

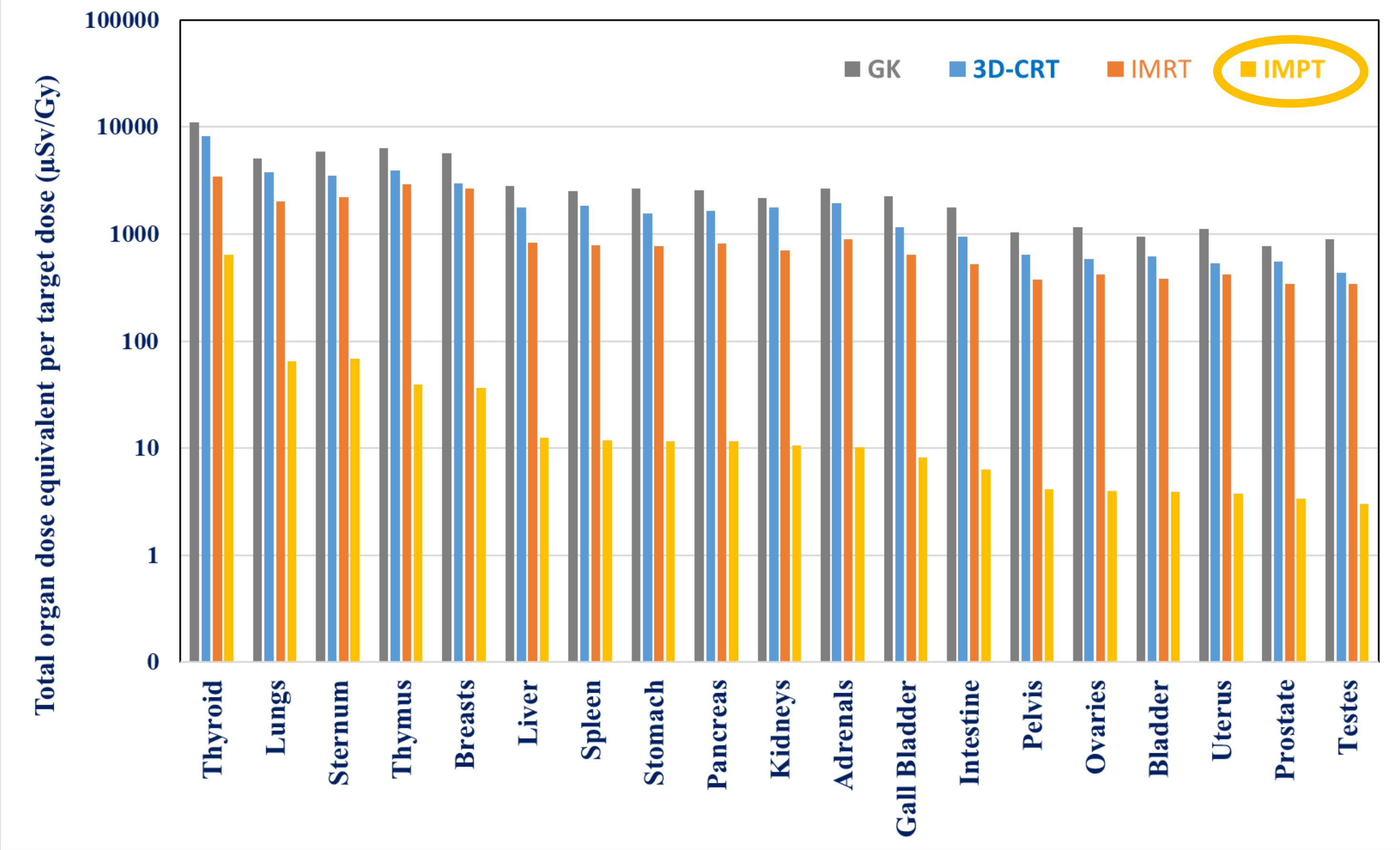

**Total organ dose equivalent**

**GK highest**
→ 11 mGy/Gy in thyroid
→ 0.9 mGy/Gy in testes

**3D-CRT lower compared to GK**
→ 8 mGy/Gy in thyroid
→ 0.4mGy/Gy in testes

**IMRT lowest doses**
→ 3.4 mGy/Gy in thyroid
→ 0.3 mGy/Gy in testes

# Proton therapy versus photon therapy (5y phantom)


**Total organ dose equivalent**

**GK highest**
→ 11 mGy/Gy in thyroid
→ 0.9 mGy/Gy in testes

**3D-CRT lower compared to GK**
→ 8 mGy/Gy in thyroid
→ 0.4mGy/Gy in testes

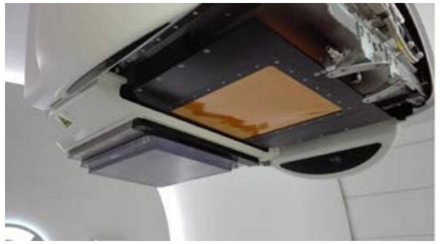
**IMRT lowest doses**
→ 3.4 mGy/Gy in thyroid
→ 0.3 mGy/Gy in testes

**IMPT lowest total doses**
- 0.64 mGy/Gy in thyroid
- 3µGy/Gy in testes

## Comparison of total absorbed organ dose for different techniques for the full treatment

| | Treatment dose | Total absorbed dose 5y | Total absorbed dose 10y |
|---|---|---|---|
| GK | for large AVM ≈ 30Gy/5 fractions | Average for both phantoms<br>344 mGy (thyroid)<br>24 mGy (testes) | |
| IMRT | For brain tumor ≈ 49Gy/25 fractions | **169 mGy (thyroid)**<br>17 mGy (testes) | **133 mGy (thyroid)**<br>9 mGy (testes) |
| IMPT | For brain tumor ≈ 54Gy (RBE)/27 fractions | **32 mGy (thyroid)**<br>0.4 mGy (testes) | **21 mGy (thyroid)**<br>0.4 mGy (testes) |


# *Out-of-field doses in proton spot scanning RT a comparison of Range shifter and 3D printed compensator*

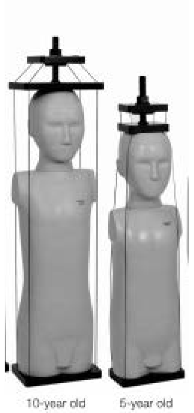


*A. Wochnik, L Stolarczyk, I. Ambrožova, M. Davídkova, M. De Saint-Hubert, S. Domanski ,C. Domingo, Ž. Knežević, R. Kopec, M. Kuc, M. Majer, N. Mojzeszek, V. Mares, I Martínez-Rovira, M. A. Caballero-Pacheco, E. Pyszka, J. Swakon, S. Trinkl, M. Tisi, R. Harrison and P. Olko, *Out-of-field doses for scanning proton radiotherapy of shallowly located paediatric tumours—a comparison of range shifter and 3D printed compensator*, Phys. Med Biol. 66 (2021)

- shallowly-located brain tumours in children
- the irradiation of superficial lesions requires the application of a pre-absorber, which reduces proton range

## Aim

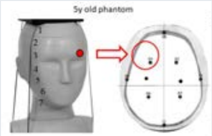
Influence of **conventionally applied RS** vs **3D printed beam compensator** on secondary radiation?


Two types of preapsorber were used:

1. RS permanently attached to the nozzle, at a distance of 46 cm from the isocentre, and can only be positioned in or out of the beamline
2. individually designed, 3D printed proton BC for 2 phantoms

**Target:** 6cm diameter sphere, shallowly located on the left-anterior side of the head



**Energy layer** ranged from **80 MeV to 140 MeV**

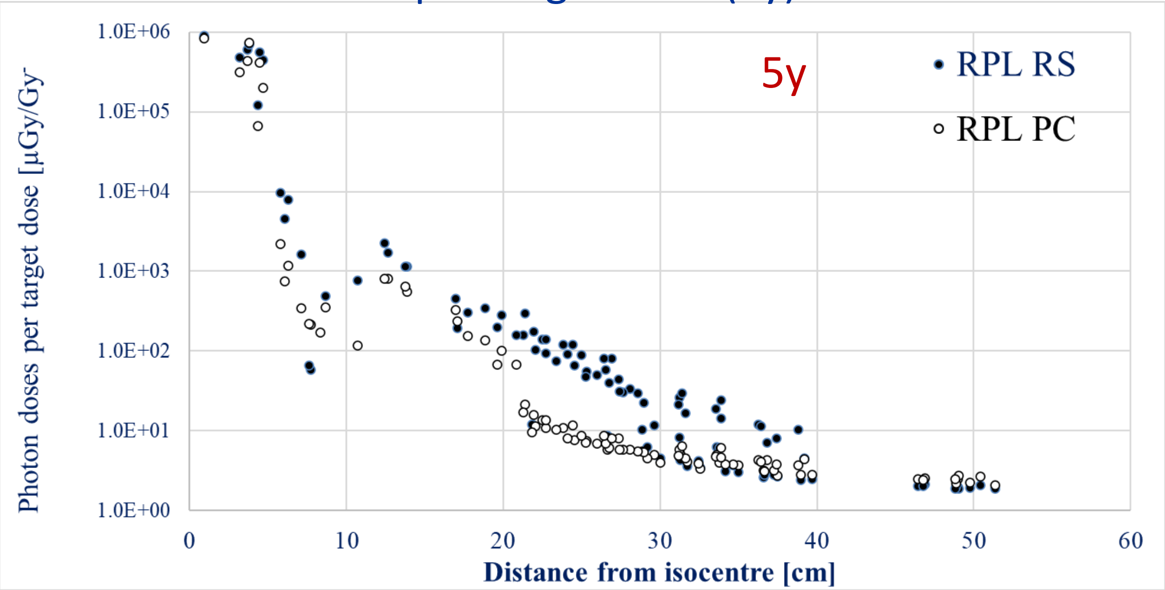
**Detectors:** TLDs, RPLs, track-etched and BD were inserted in phantom on different organ positions

# Out-of-field doses in proton RT range shifter vs 3D printed compensator

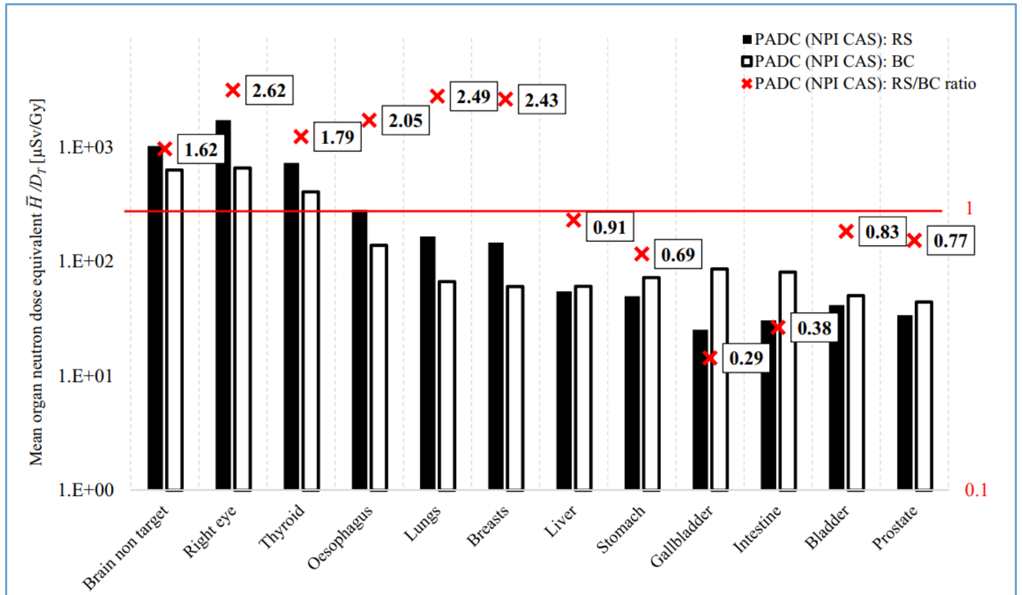
## Main findings:

- higher photon out-of-field doses for RS vs BC with the highest RS/BC ratio 12.5 and 13.2 for breasts for 5 and 10y phantoms
- For organs closest to the isocentre (thyroid), neutron doses lower for BC than RS due to neutrons moderation in the target volume, for more distant organs (bladder), lower doses for RS than BC
- Results of active measurements: dose for most of the positions determined for RS irradiations are higher than for BC by 20%–30%.

*Photon dose per target dose (5y)



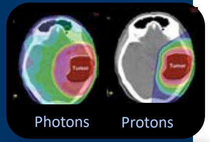

*Mean neutron dose equivalent -10y phantom




→ BC decreases out-of-field-doses compared to the RS

→ The use of RS compared to PBS without pre-absorber shows an increase of up to a factor of 2

→ use of personalized 3D printed proton compensator be can be safely used for paediatric patients




# Conclusions

- Proton PBS therapy reduced the out-of-field doses in children up to **2 orders** of magnitude when compared to photon radiotherapy techniques
- **IMPT** results in lower out-of-field doses compared to **3D-CRT, GK and IMRT** techniques (1 order of magnitude close to the brain, more than 2 orders of magnitude further away from the brain)
- The difference between photon techniques and IMPT is more pronounced for 5 y-old phantom
- Neutron doses are lower than non-neutron doses close to the target and the same time neutron doses become larger than non-neutron doses further away from the target (factor of 3-4).
- Beam modifiers used in proton PBS increase out-of-field doses up to a factor of 2
- The main dosimetric challenges remain for neutrons in proton PBS, requiring a combination detector systems to measure out-of-field doses

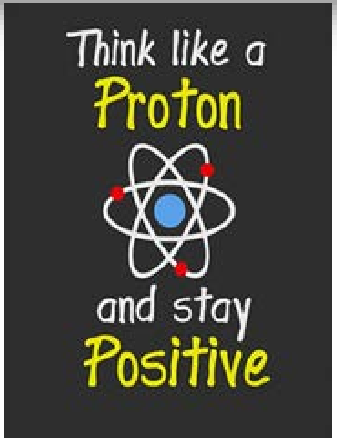
In general, out-of-field doses are required for a complete description of organ doses to RT patients – for second cancer risk estimate and other late effects as well as input to analytical models for eventual clinical implementation and for epidemiological studies

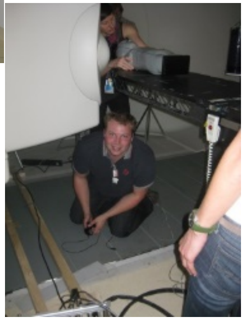
# Acknowledgments

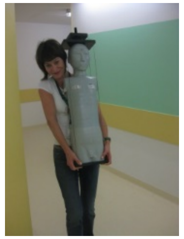

Thanks to all colleagues who prepared and participated in the experiments




Natalia Adamek
Carlo Algranati
Iva Ambrozova
Marie Davidkova
Marijke De Saint-Hubert
Carles Domingo
Vladimir Dufek
Jad Farah
Francesco Fellin
Michał Gryziński
Roger Harrison
Hrvoje Hršak
Magdalena Kłodowska
Renata Kopec
Anna Kozera
Jan Kubancak
Małgorzata Liszka
Marija Majer




Vladimir Mares
Imma Martínez-Rovira
Saveta Miljanić
Pawel Olko
Marie Romero-Exposito
Ondrej Ploc
Konstantin Schinner
Marco Schwarz
Katarzyna Skowrońska
Liliana Stolarczyk
Sebastian Trinkl
Francois Trompier
Marek Wielunski
Agnieszcka Wochnik
Filip Vanhavere