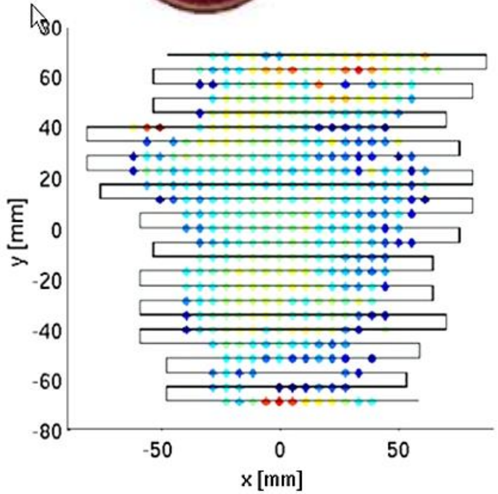

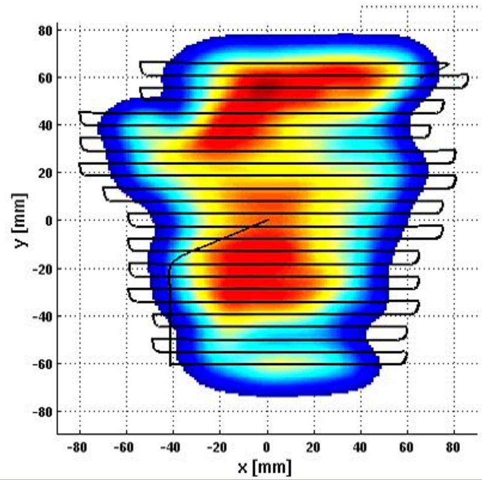

Characterization and implementation of Pencil Beam Scanning proton therapy techniques: from spot scanning to continuous scanning

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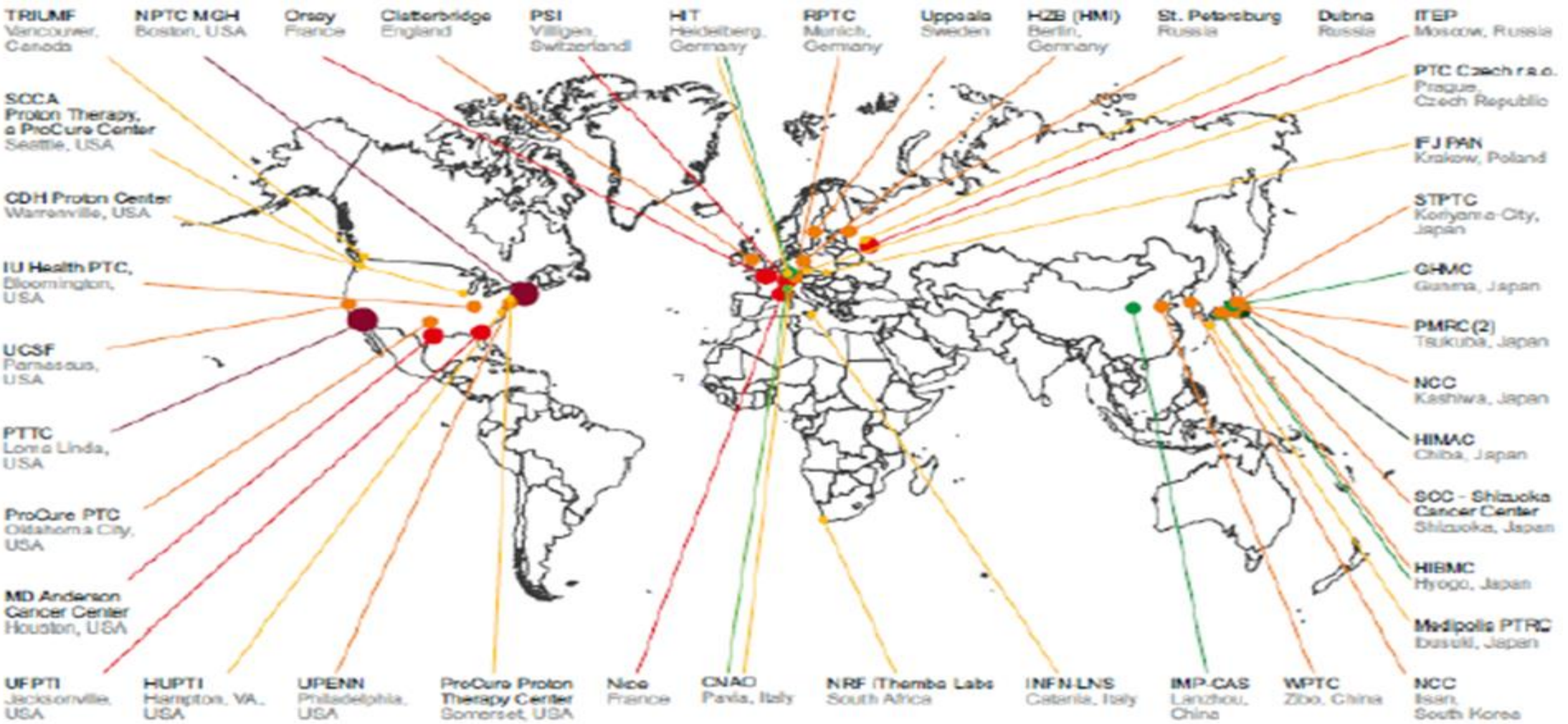
<u>Candidate</u>
Annalisa Patriarca

Outline

- Introduction
  - Physics and biology principles of protontherapy
  - Medical accelerators and delivery systems
  - Context and motivations of the PhD
- Spot vs continuous scanning
  - Dose calculations models and measurements comparisons
  - Treatment time evaluation
- Future applications of continuous scanning
- Conclusions

Introduction

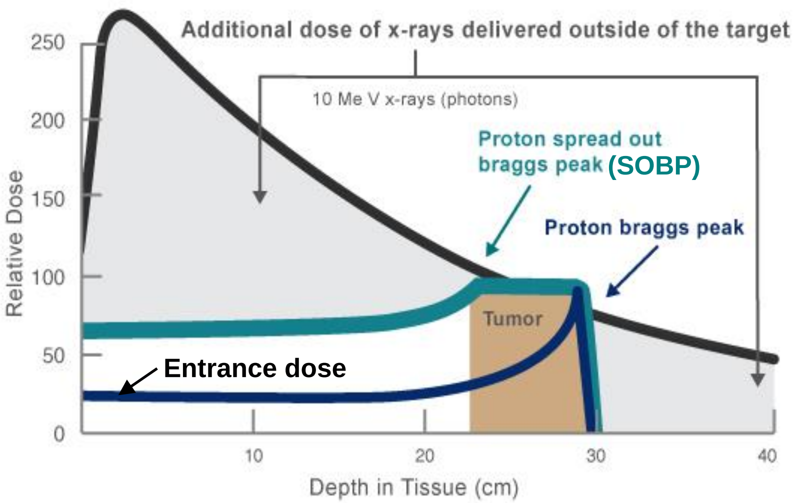


66 particle therapy facilities in operation

More then 100 expected by the end of 2020

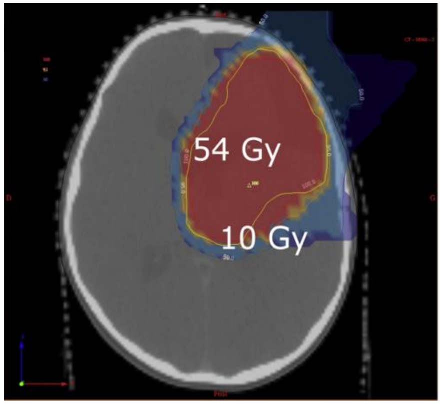
~131000 treated patients with protons (~19000 with C-ions)

Why protontherapy?

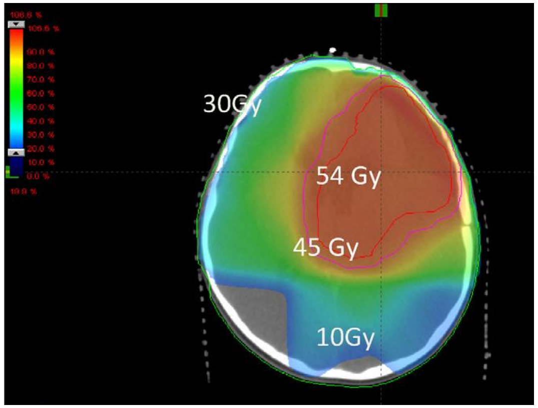


D=Evol/mvol [Gy=J/kg]

Protons dose distribution



Photons dose distribution



Max dose to the tumour ⇨ effectiveness of the treatment

Less dose to the nearby healthy tissues ⇨ toxicity limitations

Reduction of the integral doses ⇨ second cancers reduction

Higher Radiobiological Effectiveness ⇨ $RBE = \left(\frac{D_{photons}}{D_{protons}} \right)_{Survival} \cong 1.1$

- **Hadrontherapy accelerators : protontherapy solutions**

~ 60% cyclotrons wrt synchrotrons (~ 20% C-ions)

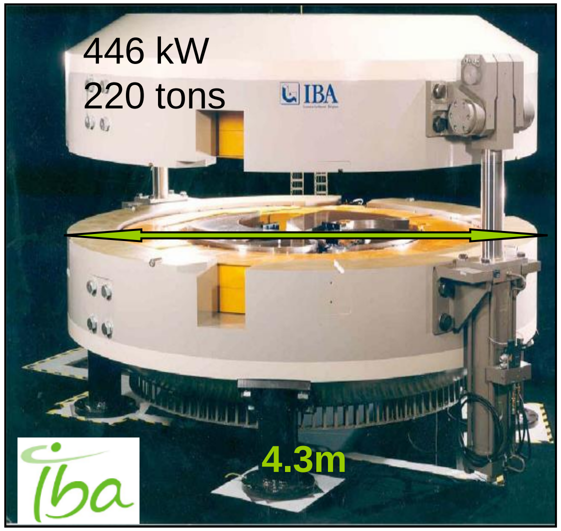
Cyclotron:

- the most compact solution

❑ **Drawback**

- fixed energy/energy degrader

Conventional cyclotron (isochronous)



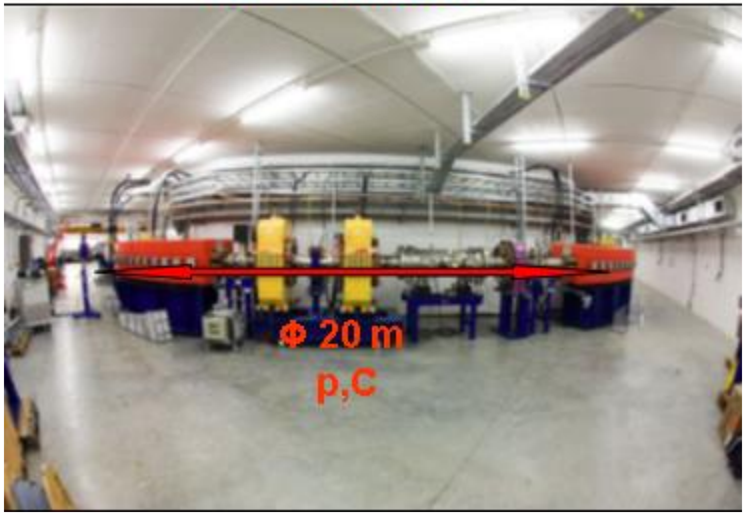
Synchrotron:

- Different particles

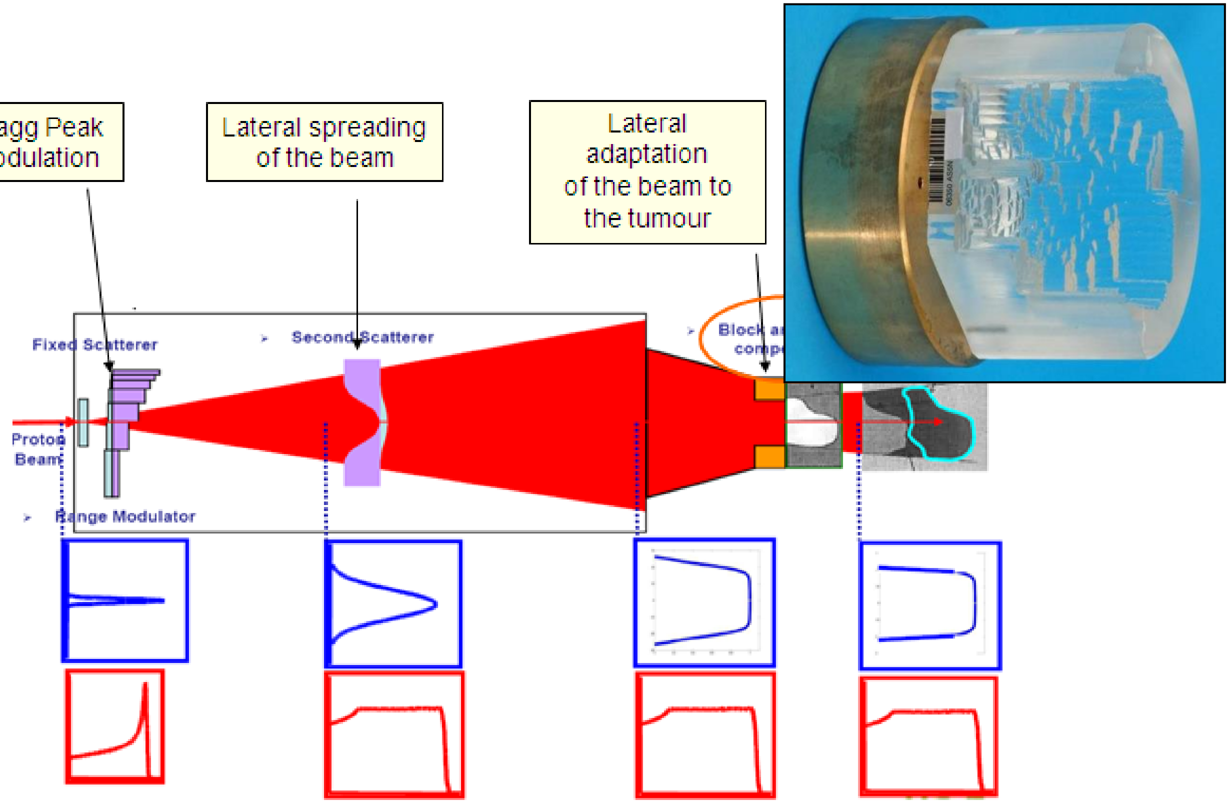
❑ **Drawback**

- Size/cost

HIT- Siemens



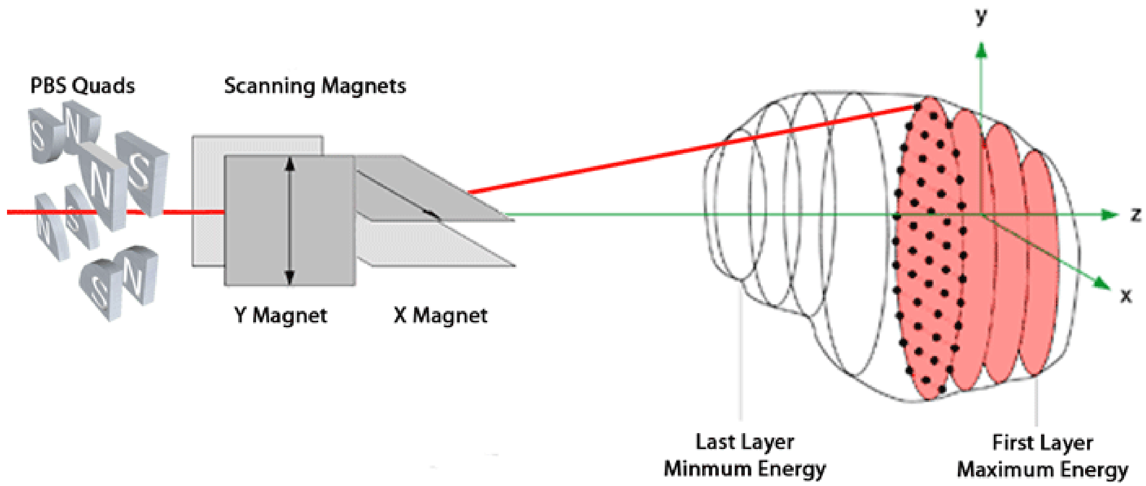
○ Delivery systems: passive spreading



- **Need for beam spreading elements to laterally and in-depth shape the beam**
- **Need for specific patient devices to conform the beam to the tumor**

○ Delivery systems: pencil beam scanning

Optimized dose distribution
- Better beam conformation
- Increase clinical indications
- The tumour is scanned through iso-energy layers

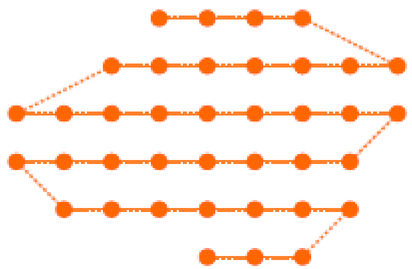


Absence of personalized accessories
- faster beam set-up
- neutron reduction at the patient level
- less radioprotection issues

○ **Delivery systems: pencil beam scanning strategies**

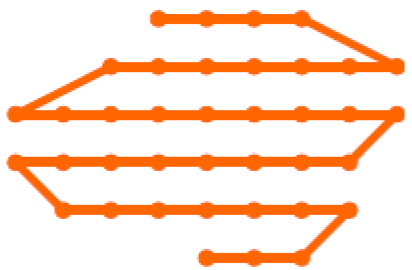
✓ Discrete dose delivery

✓ Continuous dose delivery



(a) spot scanning

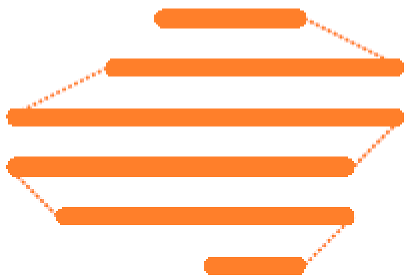
✓ Typical of cyclotrons and synchrotrons



(b) raster scanning

✓ Typical of synchrotrons

✓ Possible with cyclotrons



(c) line scanning

✓ Proposed for cyclotron in this PhD work

✓ Possible with synchrotrons

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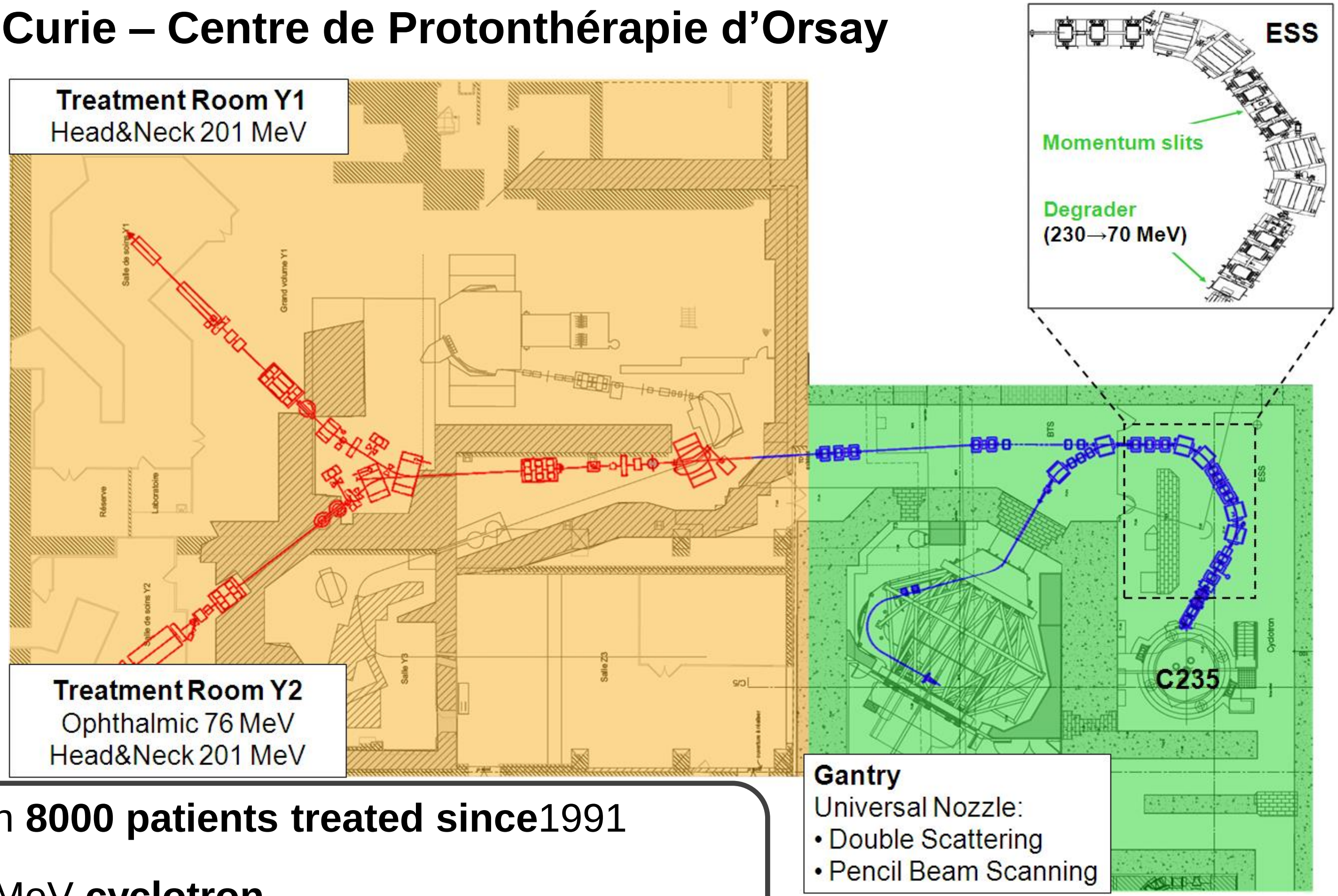
○ Context of the PhD :

Characterization and implementation of PBS proton therapy techniques at Institut Curie – Centre de Protonthérapie d'Orsay



- ✓ More then **8000 patients treated since**1991
- ✓ **IBA** 230 MeV **cyclotron**
- ✓ **3 treatment rooms**: 2 fixed horizontal and 1 gantry

○ Motivations of the PhD :

- Implementation of the **Pencil Beam Scanning** at ICPO for clinical use : data acquisition and dose modeling.

- Exploring the potential use of active scanning with the IBA system :

  - **Mobile tumors treatments** with pencil beam scanning presents the inconvenience of interplay effects due to the similar time scale between the beam delivery and the breathing cycle periodicity.

  - A **continuous irradiation** technique could be a valid solution to deliver a homogeneous dose distribution in mobile tumors cases (by speeding up the treatment time and by using repainting in a reasonable treatment duration).

  - What are the capabilities of the IBA system to perform continuous scanning irradiation pointing out what is achievable and what still need to be done.

- **High dose rate** and hypo-fractionation for **radiobiological studies**.

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Dose calculations models and measurements comparisons

- ✓ **Dose planning in protontherapy :**
  deliver Bragg peaks to cover a target volume homogeneously

Delivered dose D(x,y,z)

$$D(x,y,z) = D_{depth}(z) \times T_x D(z,\sigma_x(z)) \times T_y D(z,\sigma_y(z))$$

Depth dose (Bragg peak)

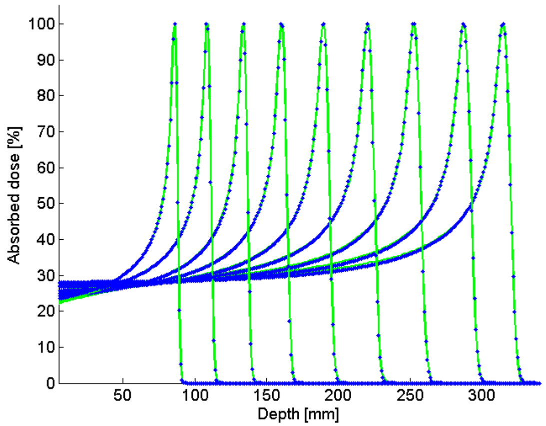
- ✓ Measurements to validate
- ✓ Analytical models
- ✓ Monte Carlo simulations

Transverse dose distributions

- ✓ Beam size (E) and divergence dependence
- ✓ Analytical models
- ✓ Monte Carlo simulations
- ✓ Measurements to characterize the beam broadening in the patient

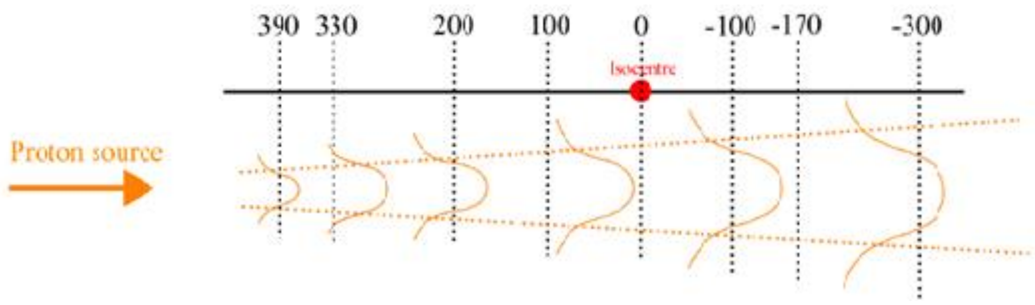
- **Dose calculations measurements**
  - ✓ Measurements device

Ionization chambers (PTW, IBA)



In water **depth-dose measurements** (green) and analytical model (blue)

Lynx : Scintillator + CCD camera

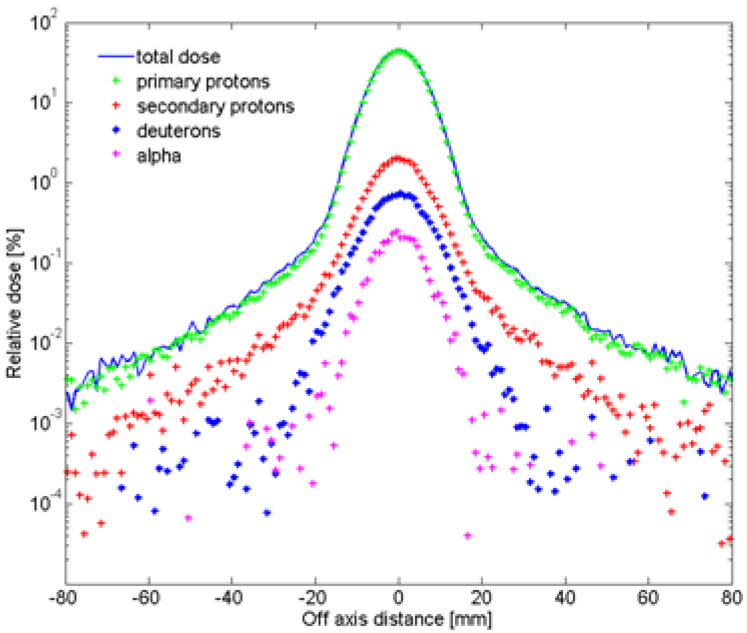


In air **spot profile measurements** set-up

- **Dose calculations models and measurements comparisons**

  - ✓ **Lateral dose : spot scanning model**

$$D(x,y,z) = D_{depth}(z) \times T_x D(z,\sigma_x(z)) \times T_y D(z,\sigma_y(z))$$



Sum of Gaussian functions

$$D(x,y,z) \sim \frac{1}{2\pi}\left(\frac{D(z)}{\sigma(z)^2} - W_2(z)\right) e^{\frac{-(x-x_0)^2-(y-y_0)^2}{2\sigma(z)^2}} + \frac{1}{2\pi}\left(W_2(z) - W_3(z)\right) e^{\frac{-(x-x_0)^2-(y-y_0)^2}{2\sigma_2(z)^2}} + \frac{1}{2\pi} W_3(z) e^{\frac{-(x-x_0)^2-(y-y_0)^2}{2\sigma_3(z)^2}}$$

Lateral dose profile of 160 MeV proton beam (sigma in air of 5 mm) in water at depth 8.5 cm. Transverse dose distribution for different secondary components are also shown. Data are from GEANT4.9.3/GATE6.2 simulations.

- **Dose calculations models and measurements comparisons**

  - ✓ **Lateral dose : continuous scanning model**

Integration of a 2D Gaussian along a straight line

$$D(x,y) = \frac{1}{2\pi\sigma_x\sigma_y}\int_A^B \mathrm{d}x' \int_{-\infty}^{+\infty} \mathrm{d}y' \delta(y' - mx' - p) \exp\left[-\frac{1}{2}\left(\frac{x-x'}{\sigma_x}\right)^2\right] \exp\left[-\frac{1}{2}\left(\frac{y-y'}{\sigma_y}\right)^2\right]$$

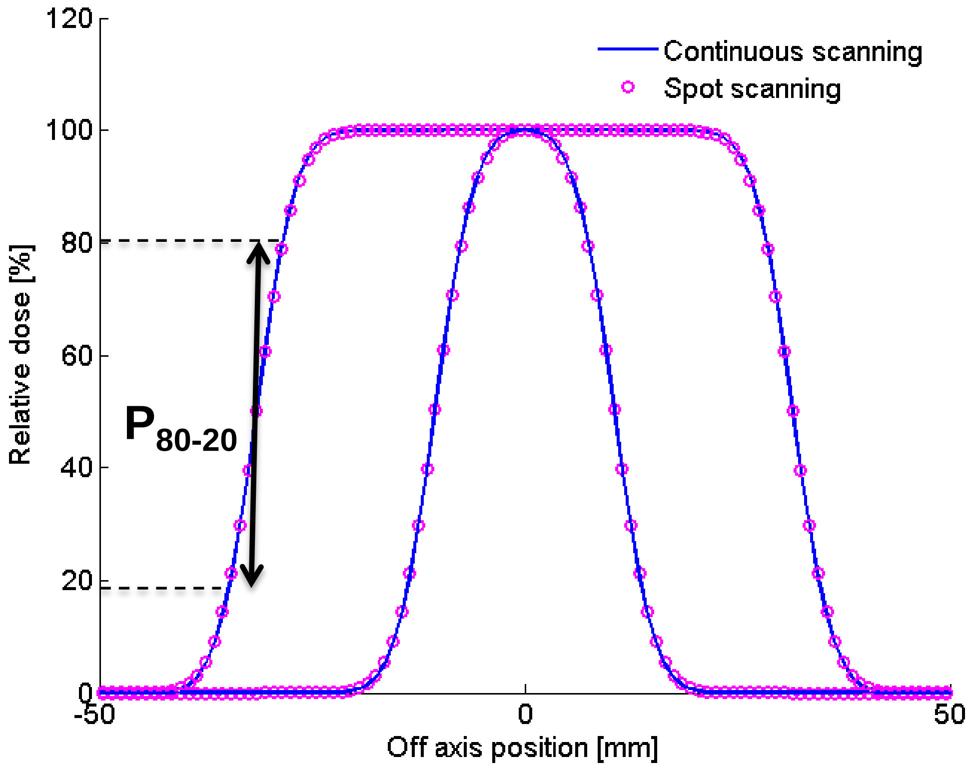
$$= \frac{1}{2\pi\sigma_x\sigma_y}\int_A^B \mathrm{d}x' \exp\left[-\frac{1}{2}\left(\frac{x-x'}{\sigma_x}\right)^2\right] \exp\left[-\frac{1}{2}\left(\frac{y-mx'-p}{\sigma_y}\right)^2\right]$$

assuming σx = σy

$$D(x,y) = \frac{1}{2\pi\sigma^2}\exp\left[-\frac{1}{2}\left(\frac{(mx-(y-p))^2}{(1+m^2)\sigma^2}\right)\right]\left[erf\left(\frac{1}{\sqrt{2}}\frac{B-m'}{\sigma'}\right) - erf\left(\frac{1}{\sqrt{2}}\frac{A-m'}{\sigma'}\right)\right]$$

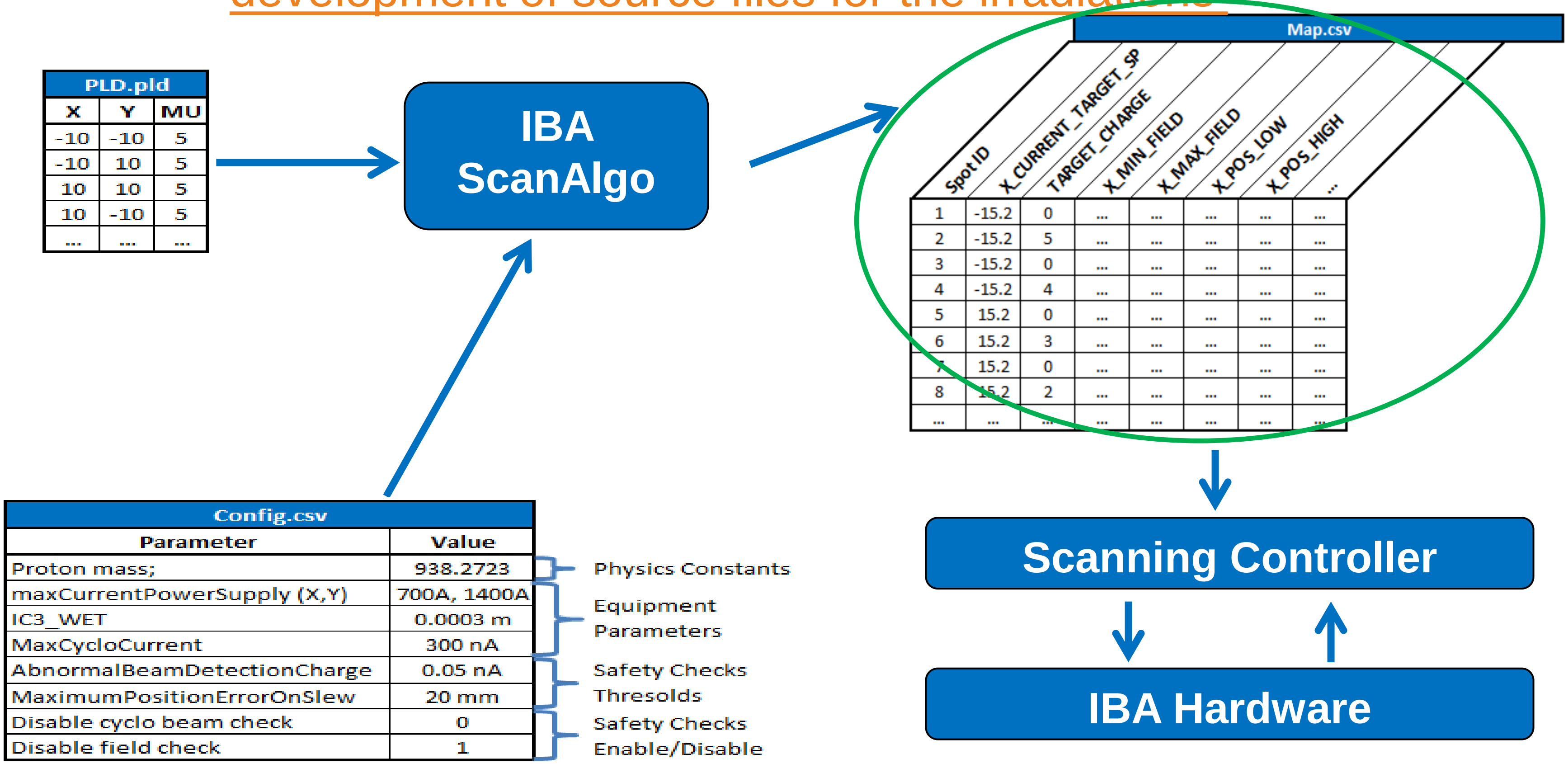
$$\sigma'^2 = \frac{\sigma^2}{1+m^2} \qquad m'^2 = \frac{x+m(y-p)}{1+m^2}$$

- **Dose calculations models comparisons : spot vs continuous**
  - ✓ **Penumbra evaluation : study on the ballistic properties of the irradiation**



- ✓ Energy dependent
- ✓ Indication of the beam enlargement due to scattering in air and patient
- ✓ Important to control the dose distribution around critical organs

- **Dose calculations measurements comparisons**
  - ✓ **How do we perform continuous measurement?**
    - study of the scanning architecture
    - development of source files for the irradiations



PLD.pld

X	Y	MU
-10	-10	5
-10	10	5
10	10	5
10	-10	5
...	...	...

Map.csv

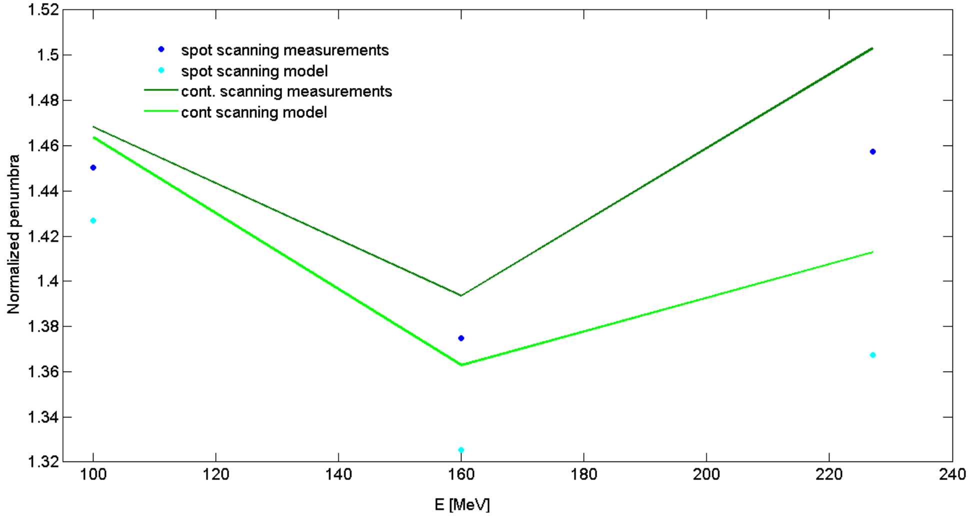
Spot ID	X_CURRENT_TARGET_SP	TARGET_CHARGE	X_MIN_FIELD	X_MAX_FIELD	X_POS_LOW	X_POS_HIGH	...
1	-15.2	0	...	...	...	...	...
2	-15.2	5	...	...	...	...	...
3	-15.2	0	...	...	...	...	...
4	-15.2	4	...	...	...	...	...
5	15.2	0	...	...	...	...	...
6	15.2	3	...	...	...	...	...
7	15.2	0	...	...	...	...	...
8	15.2	2	...	...	...	...	...
...	...	...	...	...	...	...	...

Config.csv

Parameter	Value
Proton mass;	938.2723
maxCurrentPowerSupply (X,Y)	700A, 1400A
IC3_WET	0.0003 m
MaxCycloCurrent	300 nA
AbnormalBeamDetectionCharge	0.05 nA
MaximumPositionErrorOnSlew	20 mm
Disable cyclo beam check	0
Disable field check	1

○ Dose calculations models vs measurements comparisons

✓ Penumbra evaluation : simple line



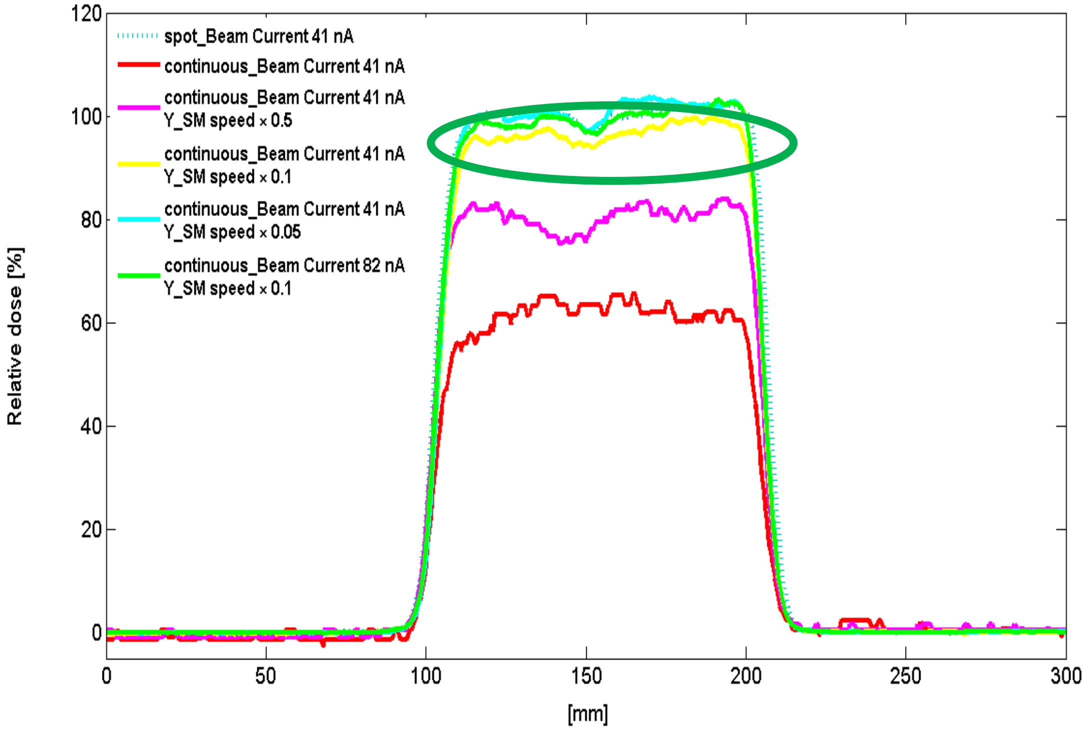
Normalized penumbras (with respect to the penumbra of a single spot) evolution with energy.

	Measurements [mm]		Models [mm]		Difference [%]	
	Spot	Cont.	Spot	Cont.	Spot	Cont.
Energy 100 MeV						
Field Size_5050	101,24	97,09				
Penumbra_8020	12,18	12,33	11,98	12,29	1,63	0,31
Energy 160 MeV						
Field Size_5050	98,81	95,76				
Penumbra_8020	8,33	8,44	8,03	8,25	3,59	2,20
Energy 227 MeV						
Field Size_5050	103,41	101,32				
Penumbra_8020	6,25	6,45	5,86	6,06	6,17	5,99

- ✓ ~6% is the maximum difference observed
- ✓ ~ 3% when only measurements are considered
- ✓ Studies on more complex cases should confirm these preliminary optimistic results on the ballistic properties of a continuous irradiation

- **Dose calculations measurements comparisons**

  ✓ **Dosimetry evaluation : defining the continuous scanning irradiation strategy to obtain the same dose for the two irradiations modalities**



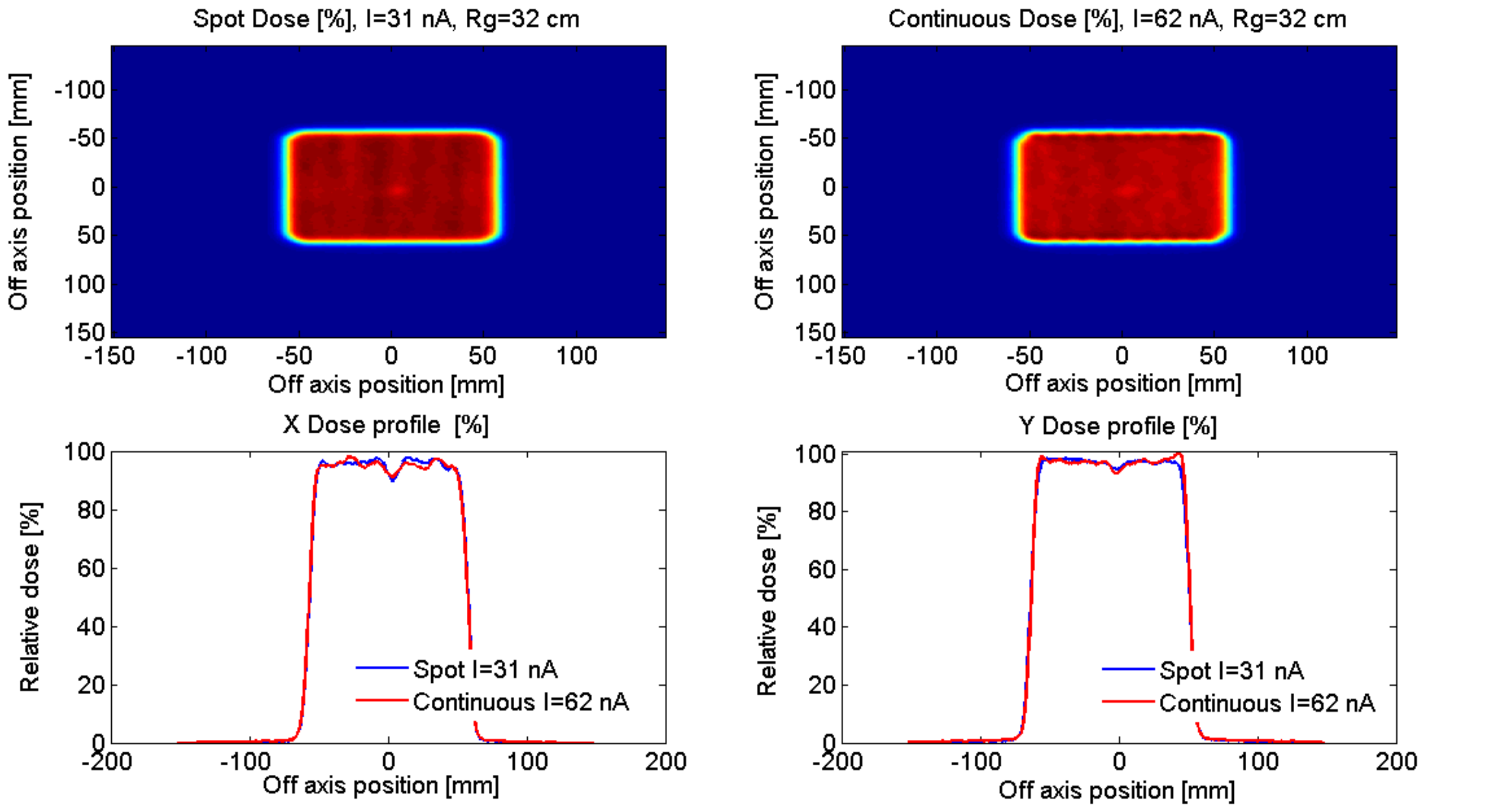
✓ **Reduce scanning magnet speed ~ 80% less**

✓ **Increase the beam current ~50% more**

Continuous irradiation strategy could be the combination of **decreasing scanning magnets speed** and **increasing current**

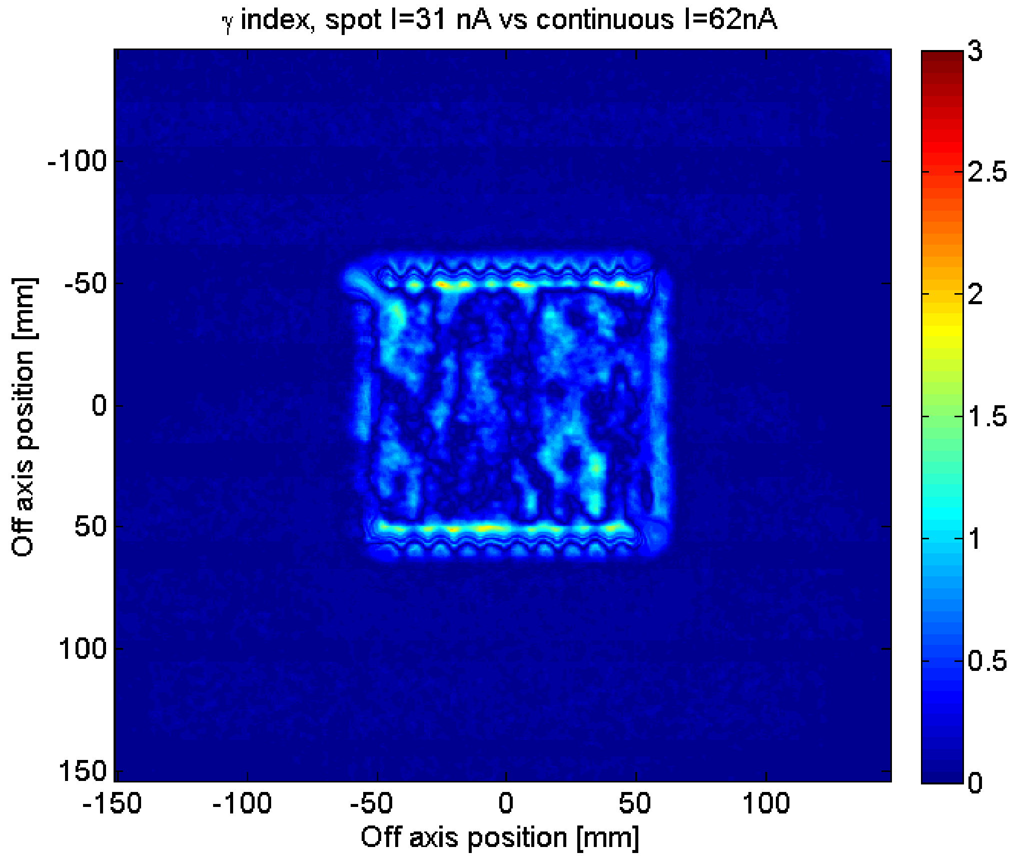
○ Dose calculations measurements comparisons

✓ **Continuous irradiation with beam current doubled wrt spot scanning case**



Dose comparison between spot and continuous irradiation at the same scanning speed and modified beam current (I_cont = 2* I_spot)).
Upper plots shows the fluence maps and lower plots are the correspondent dose profiles.

- **<u>Dose calculations measurements comparisons</u>**
  - ✓ **Gamma index (3% - 3 mm) analysis on 2D square surface**



- ✓ **Dose levels differences included in the gamma index interval**
- ✓ **Dose rate measured on the ionization chamber exceed the tolerances (> 3.5×10^{-7} C/s)**

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○ Treatment time evaluation

✓ **Development of a code to compute the total irradiation time in spot scanning**

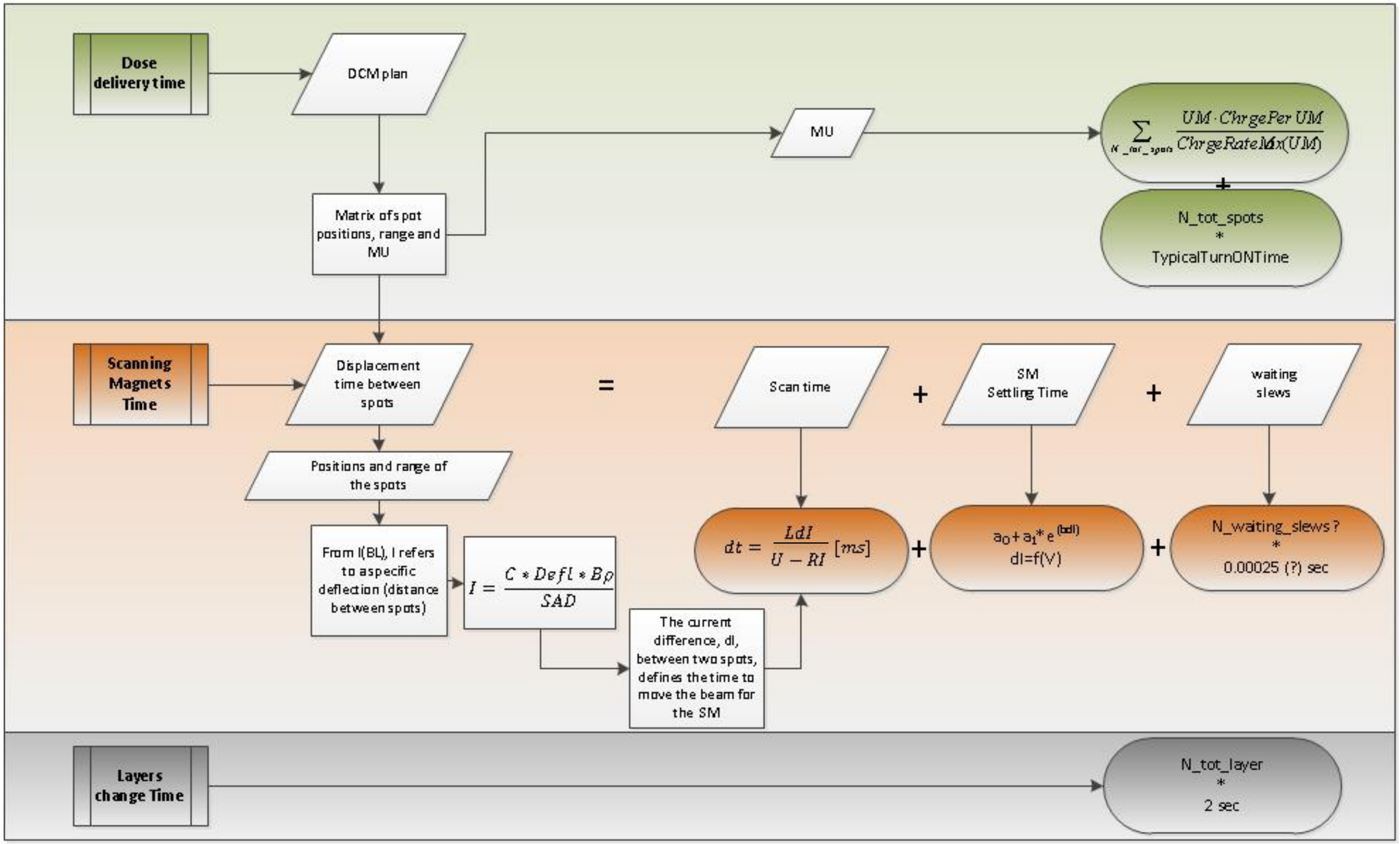
τ_{dose}

+

τ_{move}

+

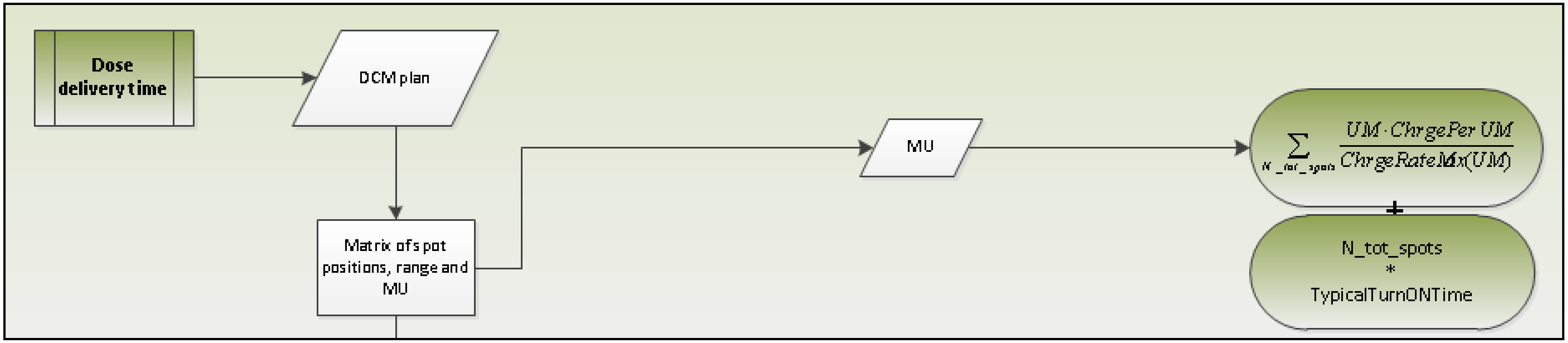
τ_{layer}



○ Treatment time evaluation

✓ **Time to deliver the dose**

$$\tau_{dose} = \frac{Q_{IC_{23}}}{\dot{Q}_{IC_{23}}}$$

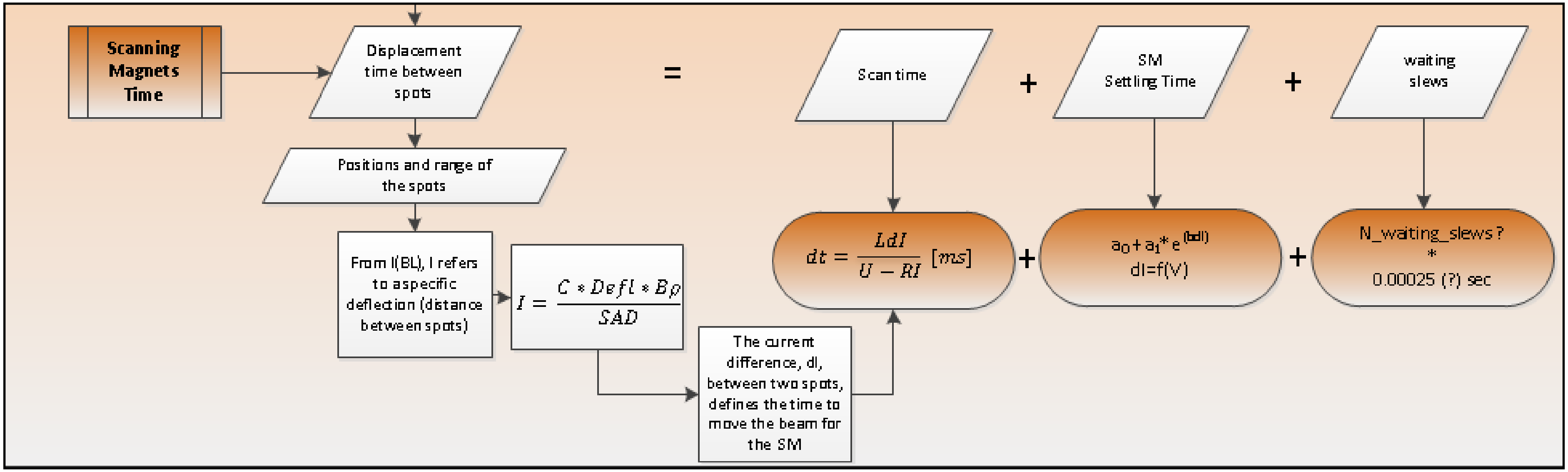


Dependence on :

- ✓ Treatment plan ⟶ Monitor Units (UM), Number of spots
- ✓ Ionization chambers charge rate reading (ChargeperUM = 1.5 nC for 1MU, ChargeRateMax = 3.5×10^{-7} C/s)
- ✓ Time to have beam from the ion source (TypicalTurnONtime = 1.5e-3 s)

○ **Treatment time evaluation**

✓ **Time to move the beam** $\tau_{move} = \tau_{scan} + \tau_{settling}$



Dependence on :

✓ Energy, spots spacing

✓ Technical specifications of the magnets (L = (0.04752,0.00474) [H], R = (0.31389,0.03658) [Ω], frequency: 30Hz e 3Hz)

✓ Feedbacks and settling times

○ Treatment time evaluation

✓ **Time to change a energy layer**

Dependence on

✓ Settling times of the beamline magnets

✓ Speed of degrader positioning

Materials and Methods

○ Treatment time evaluation

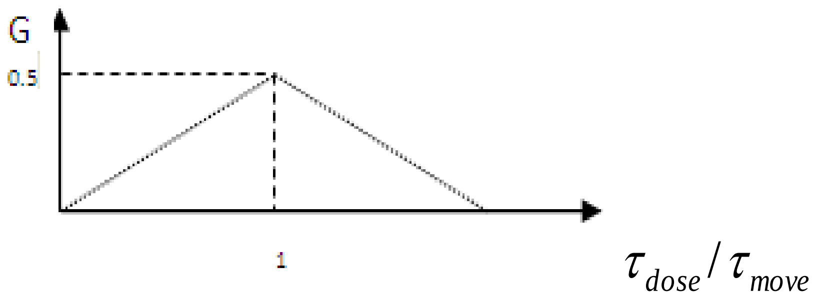
✓ Continuous scanning irradiation time

- From the spot scanning time irradiation definition

$$\tau_{total} = \tau_{dose} + \tau_{move} + \tau_{layer}$$

- Treatment time gain G factor for the continuous scanning irradiation

$G = 1 - \max(\tau_{dose}, \tau_{move}) / (\tau_{dose} + \tau_{move})$



$G = \max$, if $\tau_{dose} = \tau_{move}$

In continuous scanning the dose is delivered while moving the beam

○ Treatment time evaluation : spot vs continuous scanning

✓ Irradiation of 10 cm line

In spot scanning, $\tau_{dose} \sim 3\ \tau_{move}$, means decreasing the scanning speed and/or increasing the beam current to obtain , $\tau_{dose} \sim \tau_{move}$ and a maximum gain in continuous scanning (50%).

	Scanning conditions	Irradiation time [ms]	Gain [%]
Energy 100 MeV	Spot	155.75	
	Continuous - SM speed × 0.05 - Beam current × 1.5	89.5	42.53
Energy 160 MeV	Spot	216.5	
	Continuous - SM speed × 0.05 - Beam current × 1.07	132.5	38.8
Energy 227 MeV	Spot	313.25	
	Continuous - SM speed × 0.05 - Beam current × 1.22	185.75	40.7

✓ Measurements agree within 10% with respect to the model

○ Treatment time evaluation : spot vs continuous scanning

- ✓ Spot scanning: comparison between our code and the reference from IBA on clinical cases
- ✓ Continuous scanning model estimations
  - Dose to deliver : 2 Gy

Irradiation phases	Medulloblastoma ICPO program	Medulloblastoma IBA system	Sacrum ICPO program	Sacrum IBA system
τ_{dose} [s]	5,3	5,2	20,8	20,5
τ_{layer} [s]	78	78	92	92
τ_{move} [s]	3,1	3,4	23	24,7
τ_{total} [s]	86,5	86,6	135,8	137,3

- ✓ Differences in the two computing approaches is < 1%
- ✓ Most of the irradiation time is used to change energy layers (~67% to 90%)
- ✓ According to the model, a continuous irradiation should be around 50% faster

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- **Future applications of continuous scanning**

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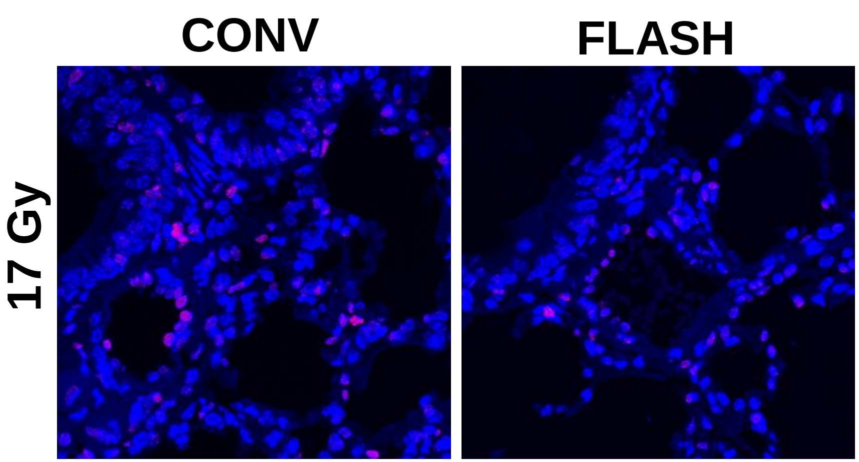
○ Future applications of continuous scanning

- ✓ **FLASH radiotherapy : dose delivery time < 500 ms and dose rate > 40 Gy/s**

Tests on mice lung tumors with a 4.5 MeV electron linac have shown:

- ✓ Same anti-tumoral efficiency and enhancement of the differential responses between normal and tumor tissues wrt CONV (dose rate < 0.03 Gy/s) radiotherapy

• Potential benefits on malignancies requiring improved tolerability of radiation:



Uveal melanoma : toxicity reduction

Gliomas : increased dose at the tumor for better local control

Increase in the cell proliferation index 3 hours after thoracic irradiation with a 200 MeV proton beam at ICPO.

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Conclusions

✓ Company – Hospital – University collaboration

✓ Implementation of Pencil Beam Scanning :

- caracterization of the established spot scanning technique for clinical use
- dose models for spot and continuous scanning
- continuous scanning irradiation strategy definition
- comparison between models and measurements : **penumbra evaluations tend to confirm a viable utilisation of the continuous approach**

✓ Treatment time in Pencil Beam Scanning :

- calculation algorithm for spot scanning : comparison with the IBA software on clinical cases : results agree within 1%
- model to evaluate the treatment time in continuous scanning
- measurements of treatment time for spot and continuous scanning : **time reduction of around 40%**

Perspectives

- ✓ Complete the evaluation of continuous scanning for more complex case
  - Dose models implementation in a Treatment Planning System
- ✓ Robustness of the technique towards mobile tumors treatments
  - Industrial work on energy layer time reduction
  - Dose monitoring improvement to allow a safe continuous irradiation
- ✓ Biological caracterization of high dose rate irradiation
  - if a constraint on irradiation time is assessed to be beneficial on healthy tissues while treating cancer, continuous irradiation could be a solution to treat a large volume in shorter time compared to spot scanning (e.g. in FLASH radiotherapy)

GRAZIE