

31.Aug.2019



# TPS transition of dose calculation method and state of the art of Planning System



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National Cancer Center Hospital East, Japan



# Outlines



- About National Cancer Center Hospital East
- About TPS: State of the Art

## **Introduction of Our Proton TPS**

- Simplified Monte Carlo for Broad Beam
- Independent Dose Calculation for Patient QA

# National Cancer Center Hospital East

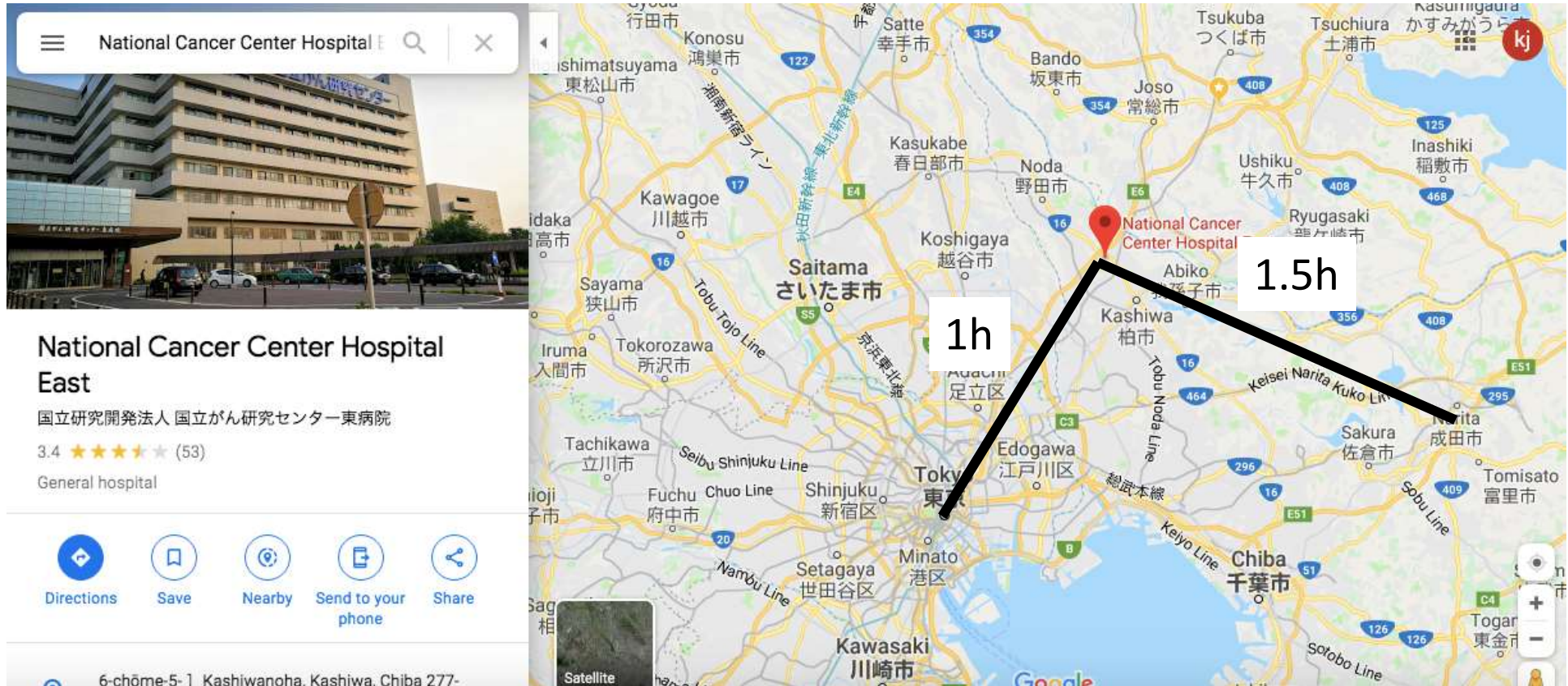
**National Cancer Center Hospital East**  
国立研究開発法人 国立がん研究センター東病院  
3.4 ★★★★★ (52)  
General hospital

Directions Save Nearby Send to your phone Share

- 6-chōme-5-1 Kashiwanoha, Kashiwa, Chiba 277-8577
- 〒277-8577 千葉県柏市柏の葉6丁目5-1
- WW2R+FG Kashiwa, Chiba
- ncc.go.jp
- 04-7133-1111
- Open now: 8:30AM–5:15PM

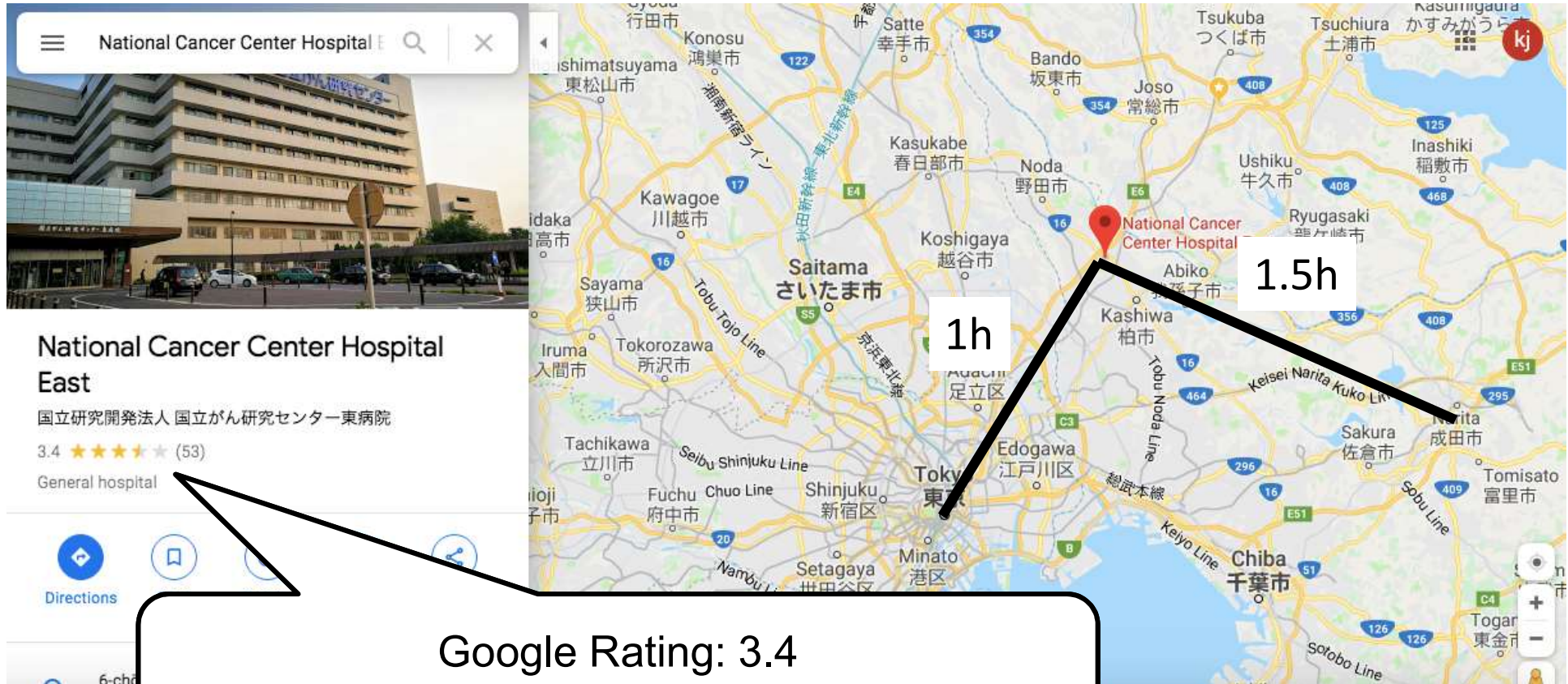
Map data ©2019 Google, SK telecom, Japan, Terms, Send feedback, 500 km

# National Cancer Center Hospital East





# National Cancer Center Hospital East



Google Rating: 3.4

≒Average value of hospitals in Japan



# Machines



## 4 Lineacs

- ONCOR (Siemens)
- Clinac-iX (Varian)
- TrueBeam (Varian)
- Halcyon (Varian)

## 2 Proton Gantries

- Proton G1 (Sumitomo)
- Proton G2 (Sumitomo)

## No Brachytherapy

Once Closed, Restart in 2020

## TPS

- RayStation (ReySearch):X
- Eclipse (Varian):X,P
- PTPLAN (in-house):P
- ~~XiO(Electa)~~

## Support System

- MIM maestro (MIM software)

## CT

- Aquillion One (Canon)

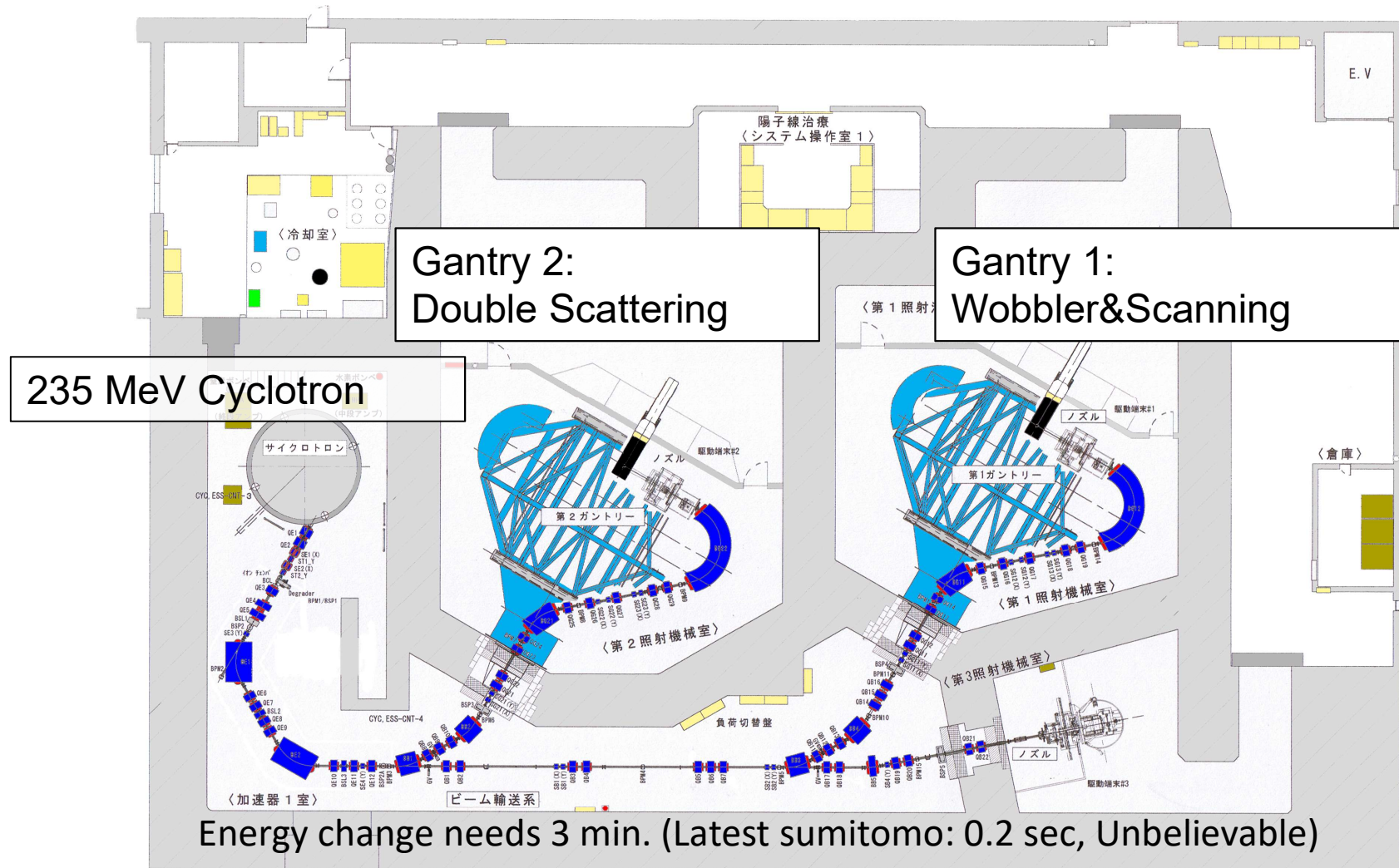
## Staff (Photon + Proton)

- Physician : 7 (+2 Part-time)
- Therapist: 18
- Medical Physicist : 5(+4 Part-time)
- Nurse: 3





# Proton Therapy System

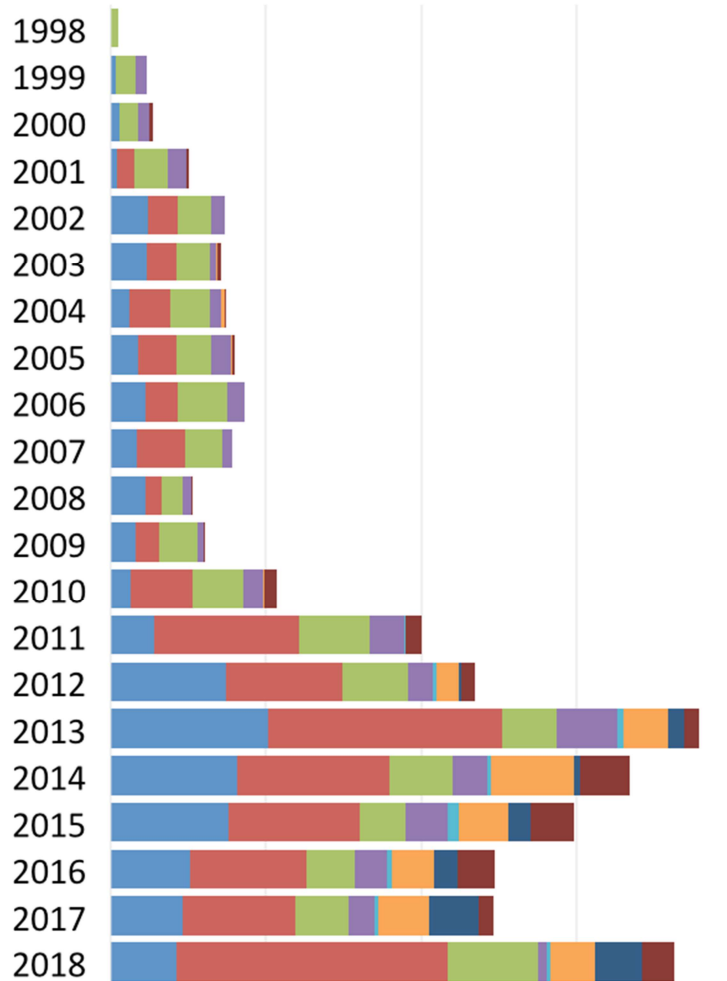




# Proton therapy

Number of patient

0 100 200 300 400



- 1998. First Treatment

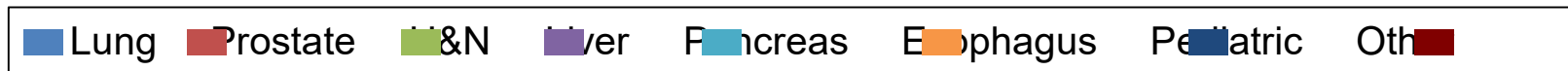
Customizing for Scanning

- 2014.10. First Scanning Treatment

(Only Prostate)

- 2018.09. Using Eclipse for scanning

- 2018.10. IMPT(Head and Neck)





# Outlines



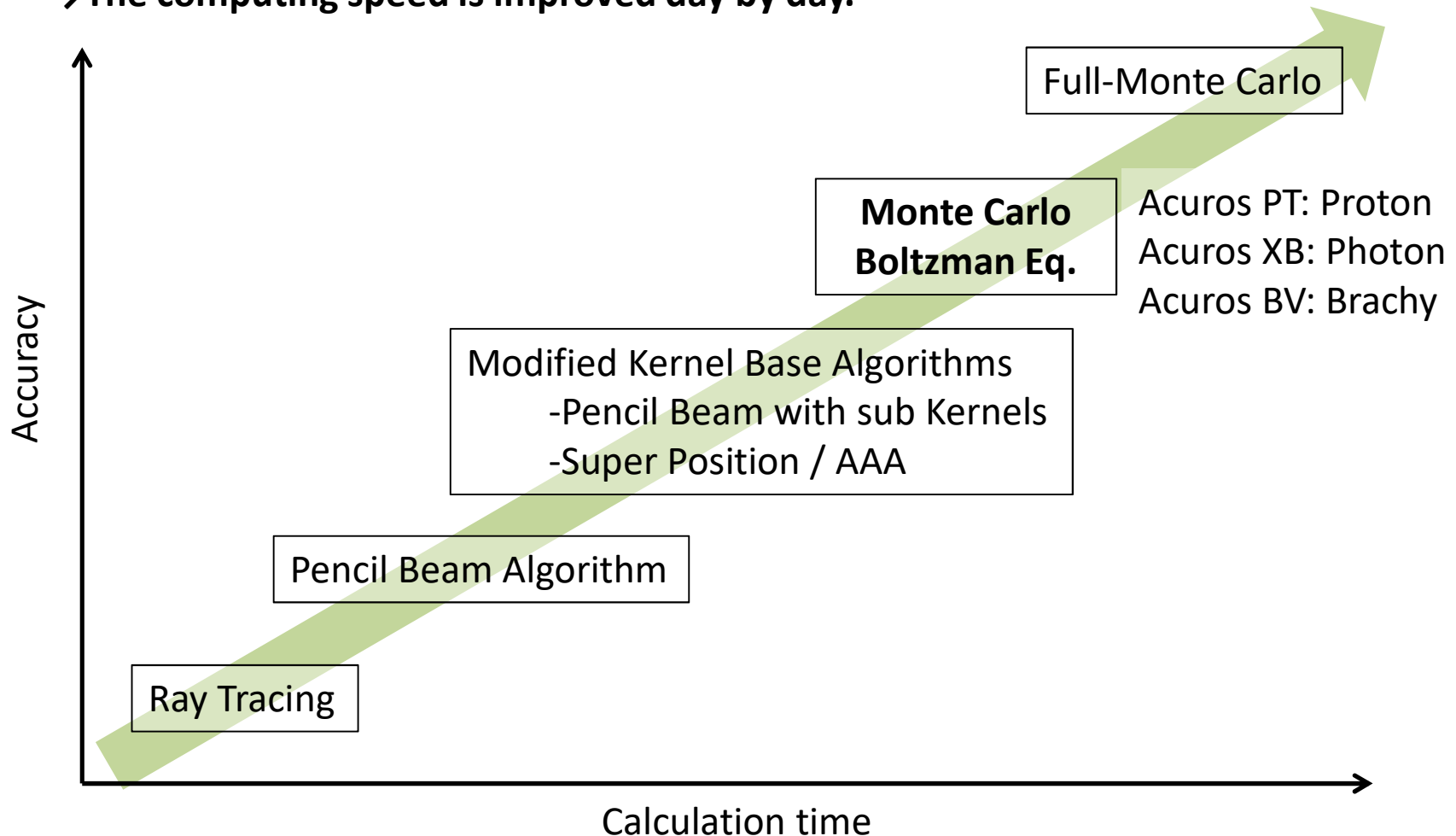
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- About TPS: State of the Art

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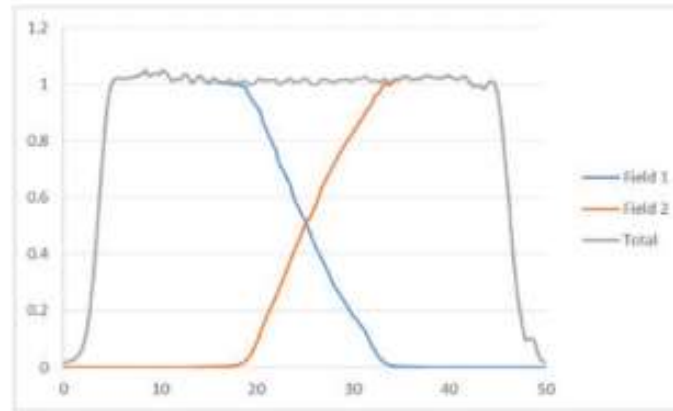
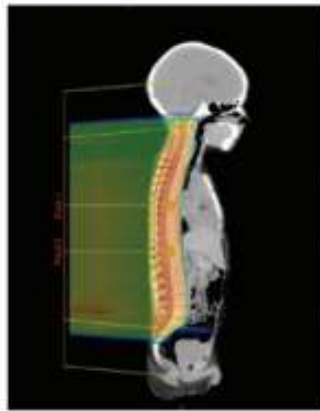
# Evolution of Calculation Algorithm

Accurate algorithm needs LONG calculation time  
→The computing speed is improved day by day.

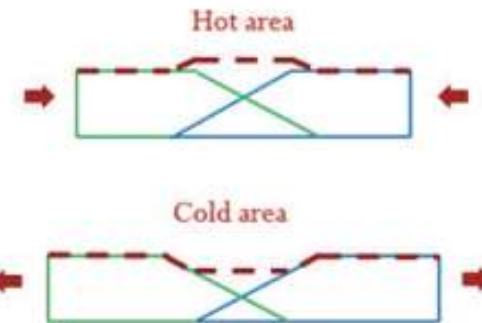
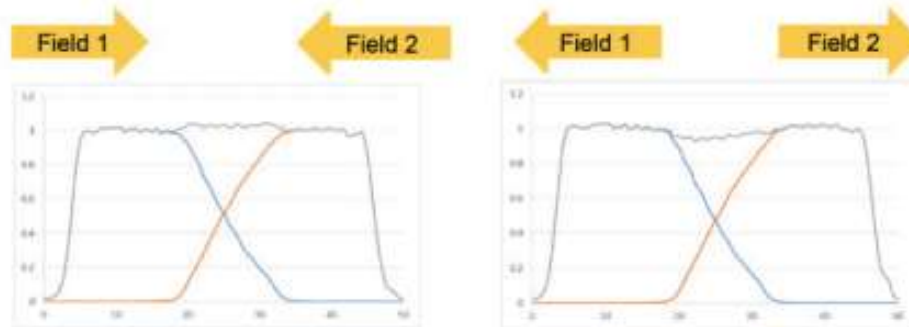


# Robust Optimization

Dose profile of robust IMPT plan for CSI



Robust analysis of robust IMPT plan for CSI



The impact of robust junctions on a plan with two beams and two isocenters (image courtesy of: MD Anderson Cancer Center)



# Automation



Improving Health  
Through Medical Physics

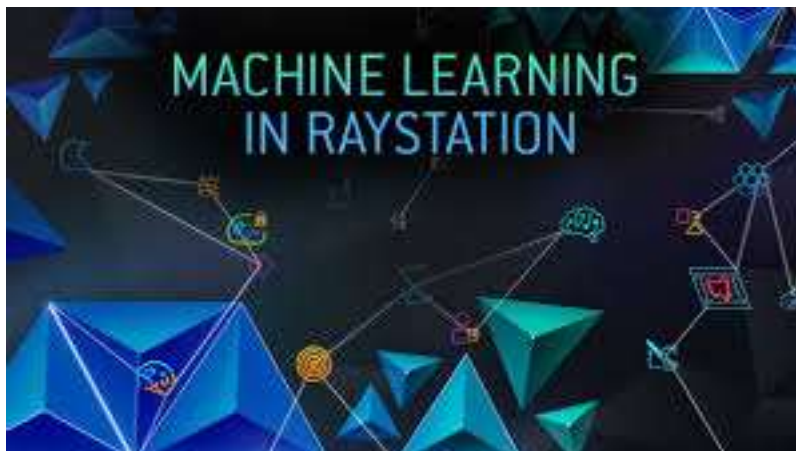
Login

AAPM

## AAPM VIRTUAL LIBRARY

2016 AAPM Annual Meeting - Session: An Introduction to Research and Clinical Development Using Treatment Planning System APIs

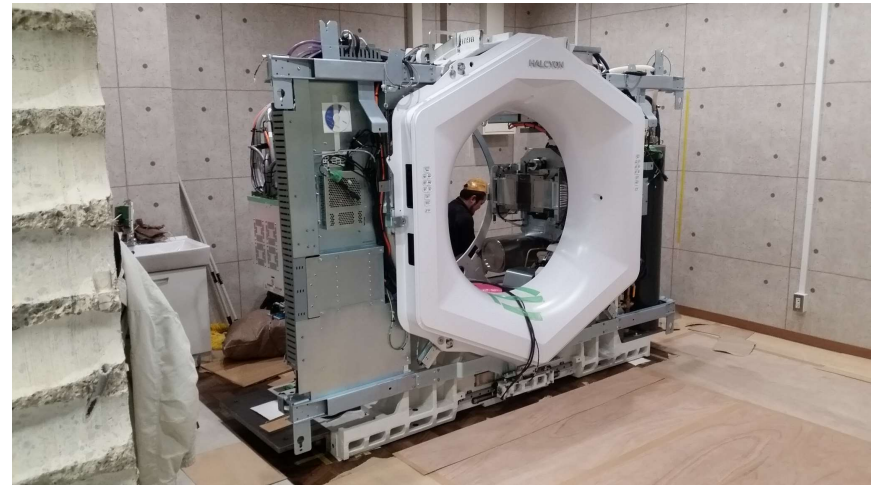
Home | Directory | Career Service:  
Continuing Education | BBS | Cont



- Session about TPS APIs (Application Programming Interface) Some codes are uploaded on git-hub.
- Machine learning for Auto Planning

## Golden Beam Data

- Varian has been provides **GOLDEN BEAM DATA** (Averaged beam data)  
→ User can start RT without measuring beam data.
- Halcyon: User **can't** touch the beam data.  
Varian certifies the beam data.



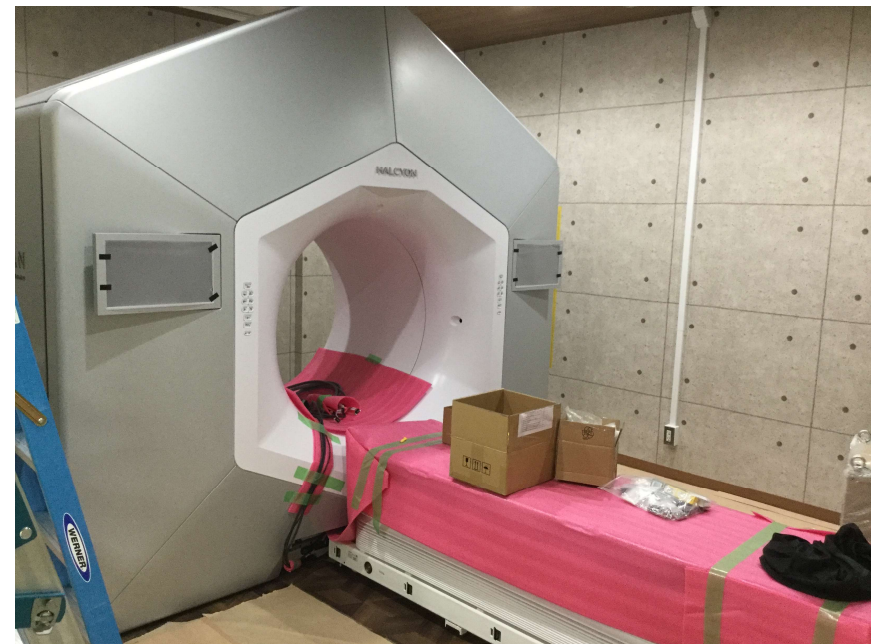
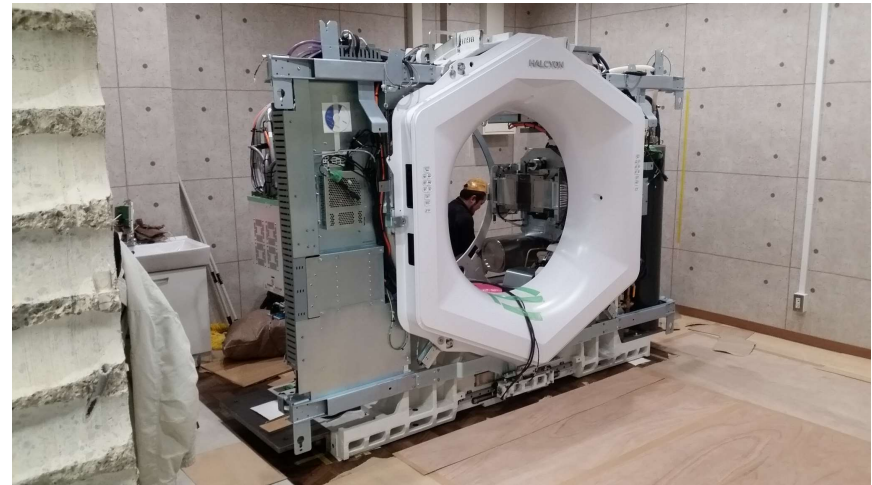
# Machines

There is 3% dose output error.

Beam data are protected.

We fixed error by modifying  
output factor calibration.

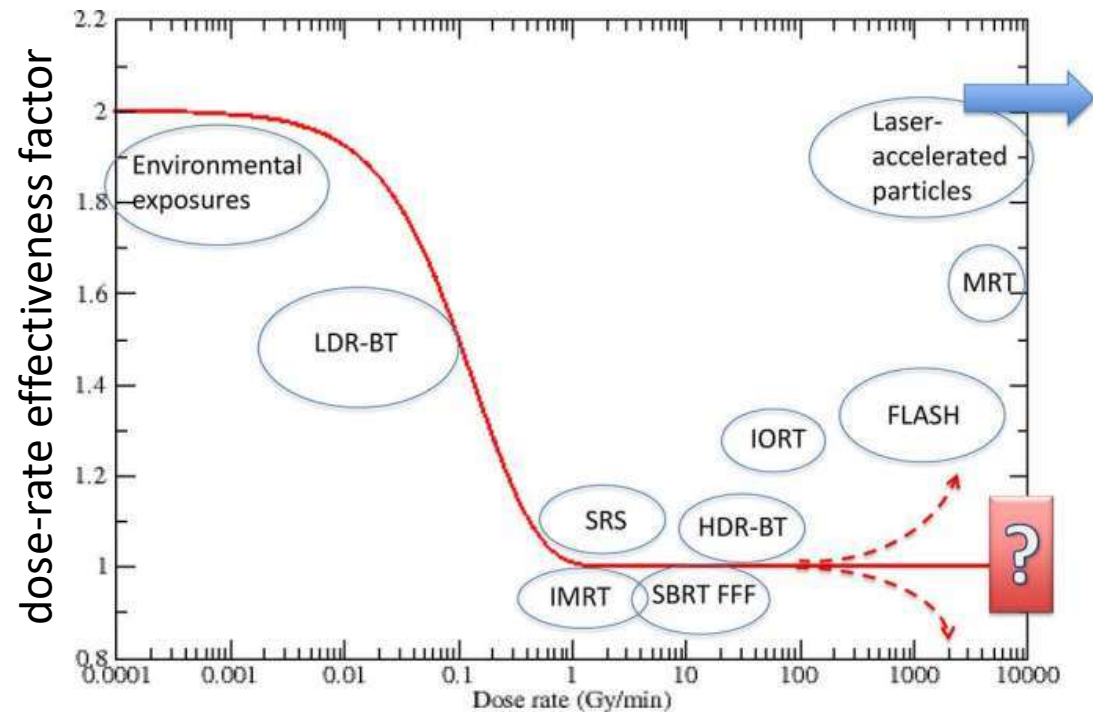
**Negative image for Halcyon.**



# FLASH: ultra high dose rate RT

Science Translational Medicine 16 Jul 2014 Vol. 6, Issue 245, p245

- NTCP is decreased at dose rate  $> 30$  Gy/sec.
- This phenomenon is only occurred *in vivo*, not *in vitro*.
- It is hard to believe, but there is dream in the result.





# FLASH: ultra high dose rate RT

Proton therapy / 11.06.2019

## Successful Ultra High Dose Rate delivered at Isocenter in IBA's compact proton therapy solution

Louvain-la-Neuve, Belgium, 11 June 2019 – IBA (Ion Beam Applications SA), the world's leading provider of proton therapy solutions, is pleased to announce the first Flash irradiation in an IBA Proteus@ONE compact gantry treatment room at the Rutherford

Cancer Cent  
represents a  
their work to

## Varian Forms FlashForward Consortium to Study Ultra-high Dose Rate Cancer Treatments with Protons

October 20, 2018

PALO ALTO, Calif., Oct. 20, 2018 /PRNewswire/ -- To expand the encouraging preclinical and translational research already conducted by Varian (NYSE: VRSN) and its clinical partners, Maryland Proton Treatment Center, the University of Maryland System Proton Therapy Center, on the value of ultra-high dose rate FLASH proton therapy for cancer, the company has formed the FlashForward Consortium. Composed of initial thirteen members, the consortium is focused on preclinical research, clinical implementation and advocacy efforts of Flash therapy. The initial FlashForward Consortium members are:

**Commercial purpose?**

# FLASH: ultra high dose rate RT

Dr. Montay-Gruel P, Radiother Oncol. 2018 Dec;129(3):582-588

X-rays can trigger the FLASH effect: Ultra-high dose-rate synchrotron light source prevents **normal brain injury after whole brain irradiation** in mice.

Whole Brain irradiation is needed for

- Small cell lung cancer
- **Pediatric** neuroblastoma.

Side effect: Decrease learning ability.



# Outlines



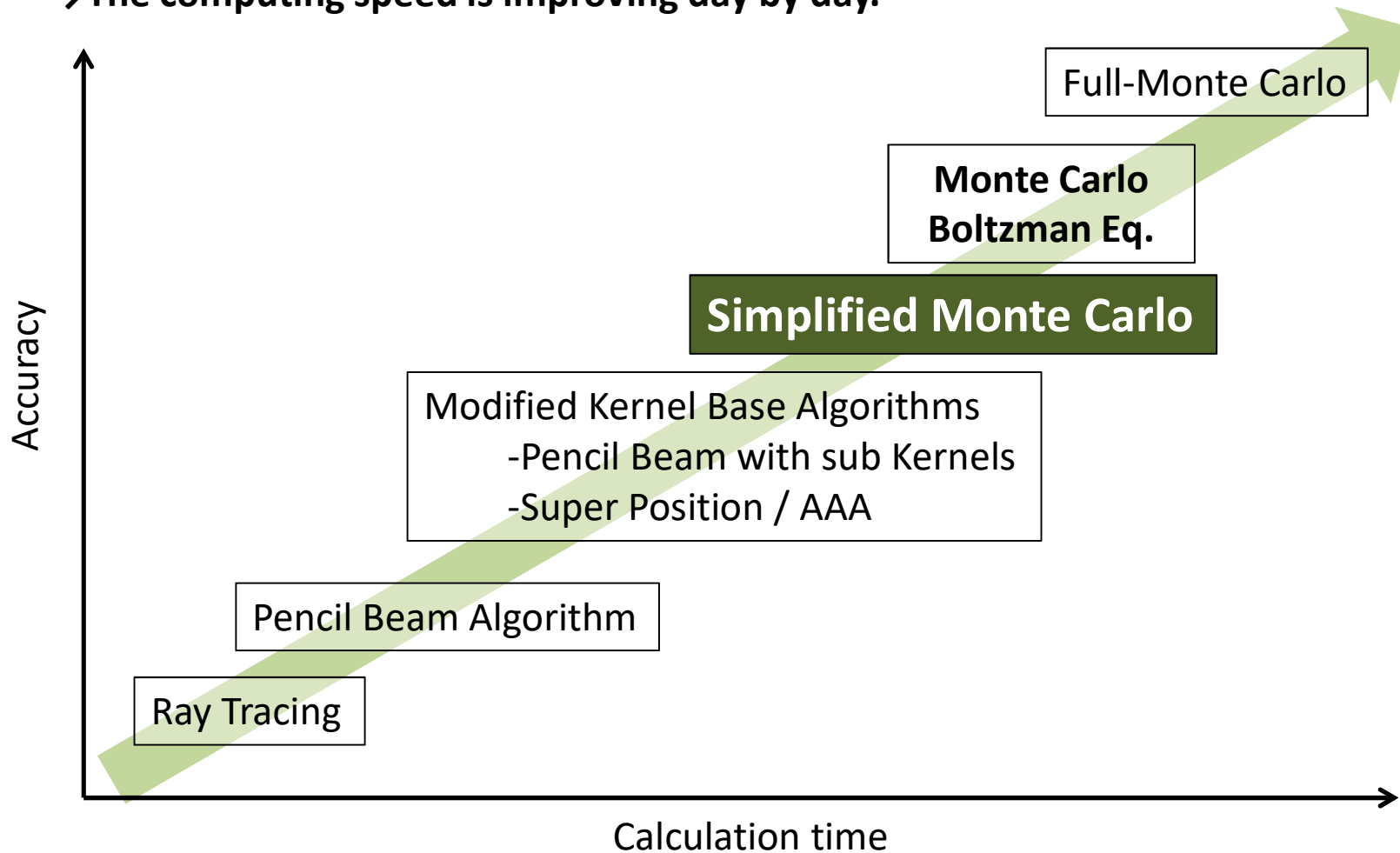
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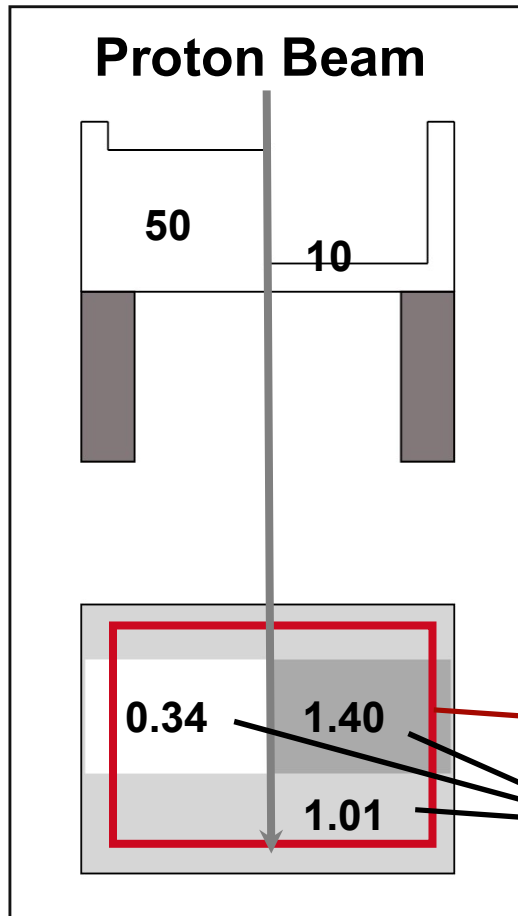
# Simplified Monte Carlo

Accurate algorithm needs long calculation time  
→ The computing speed is improving day by day.





# Why does PBA failed the calculation?

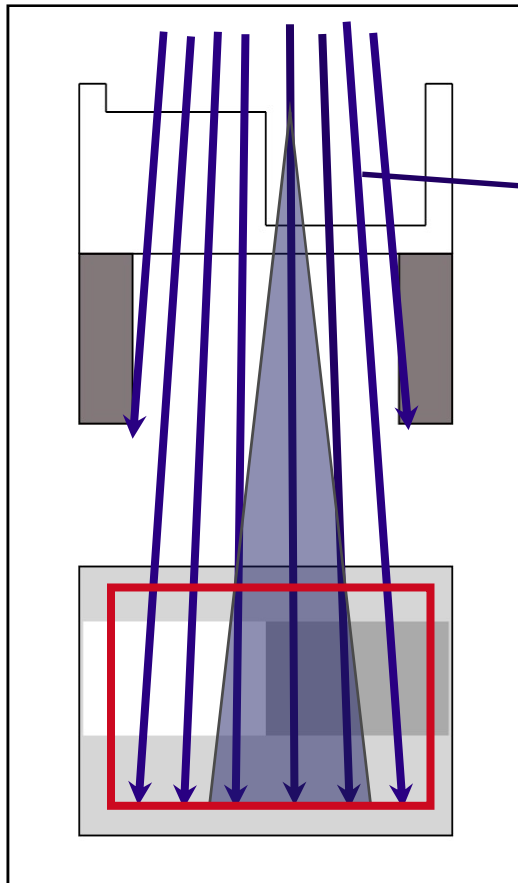


Assuming slab geometry

Target Region

Water Equivalent Thickness Ratio

# Why does PBA failed the calculation?



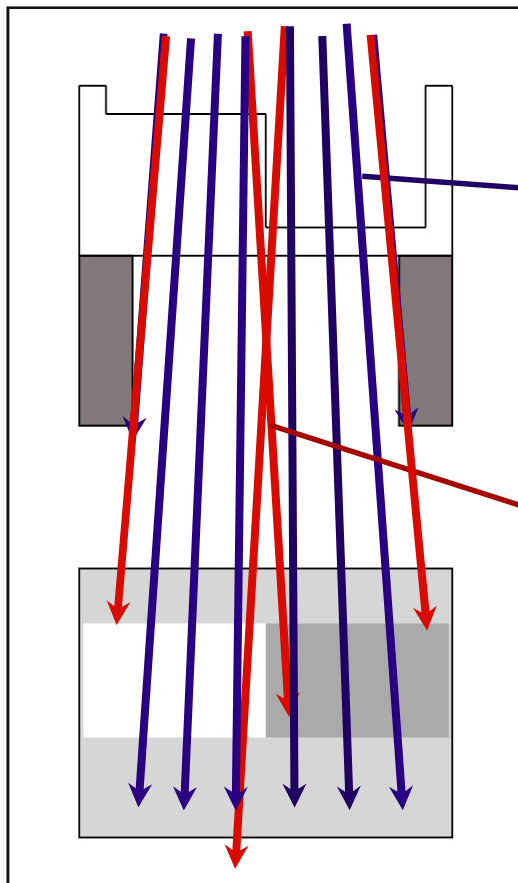
## PBA

The Central Axes of Pencil Beam kernels

- Straight Lines from the Beam Source
- Vanish in the collimator
- Initial Parameter : Effective Source Model
- Lateral Scattering : Highland's eq.
- Energy Loss : Water Equivalent Model
- Dose Deposit : Measured Depth Dose

L. Hong et al; Phys. Med. Biol. **41** (1996)

# Why does PBA failed the calculation?



The Central Axes of Pencil Beam kernels

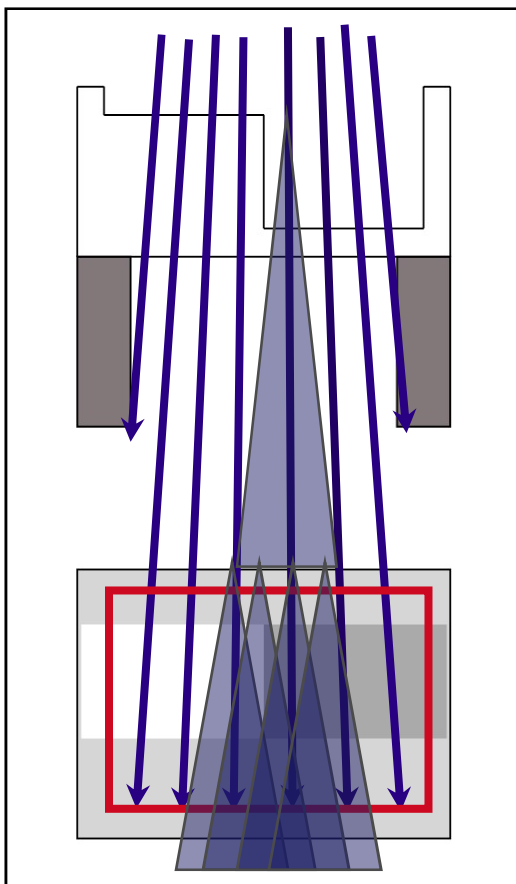
□ Straight Lines from the Beam Source

□ Vanish in the collimator

PBA missed these Paths

→ forms Higher/Lower Dose Regions

# Why does PBA failed the calculation?



To avoid ignored path...

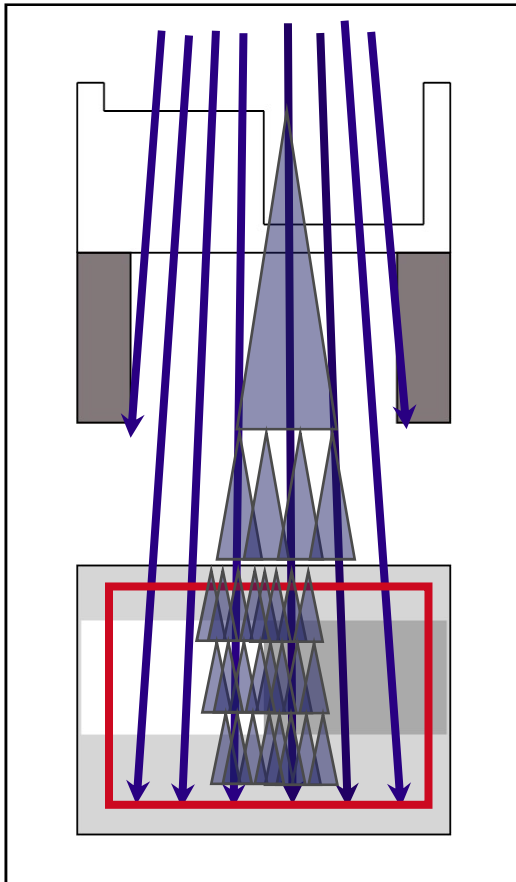
**Modified PBA**

**Divide kernels into sub-kernels.**

→ **Installed in Eclipse**

Schaffner B, Phys. Med. Biol. 44; p27 (1999)

# Why does PBA failed the calculation?



To avoid ignored path...

Divide kernels more multiply



Calculate Multiple Integrals



Increase the Calculation time

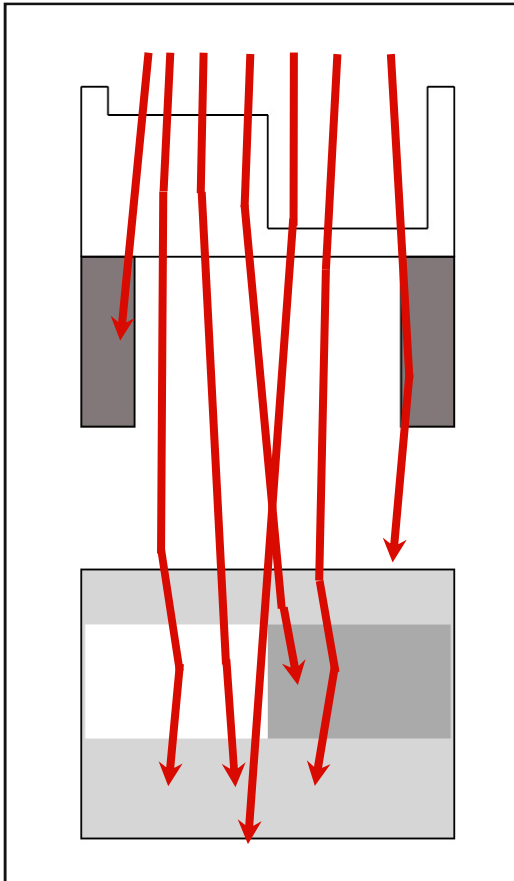
Calculate the multiple integrals

in realistic time

= Primitive Aim of Monte Carlo



# Simplified Monte Carlo



**The SMC traces individual proton path**

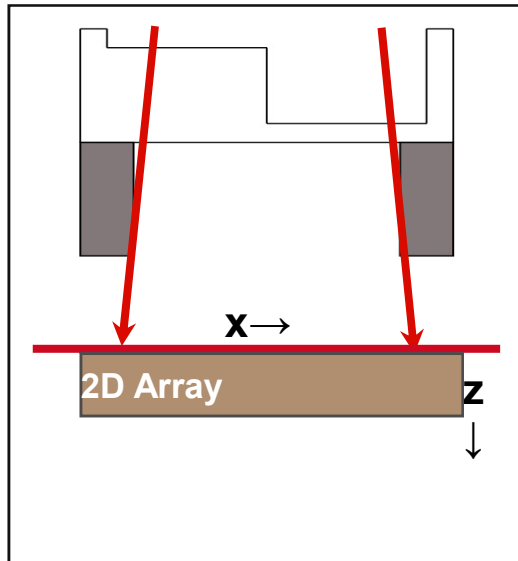
- Initial Parameter : Effective Source Model**
- Lateral Scattering : Highland's eq.**
- Energy Loss : Water Equivalent Model**
- Dose Deposit : Measured Depth Dose**

Hotta K, Phys. Med. Biol. 55; p3545-3556 (2010)

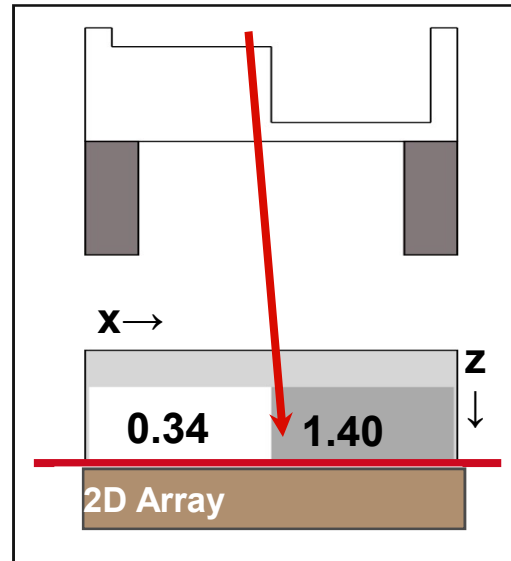
# Verification in slab phantom

Detector : PTW Octavius

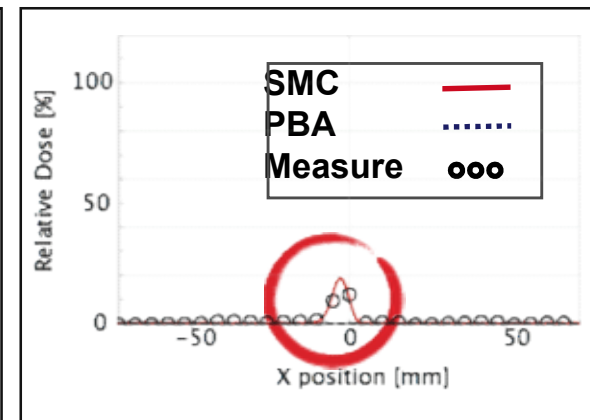
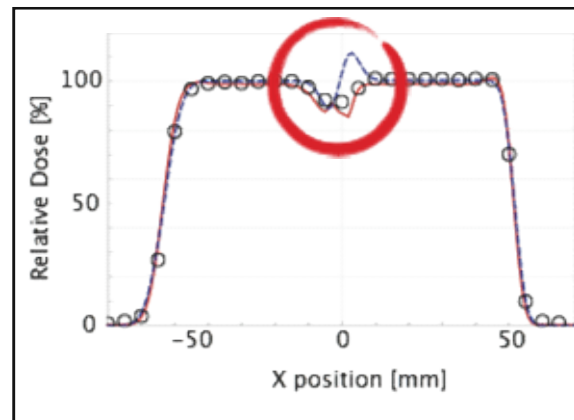
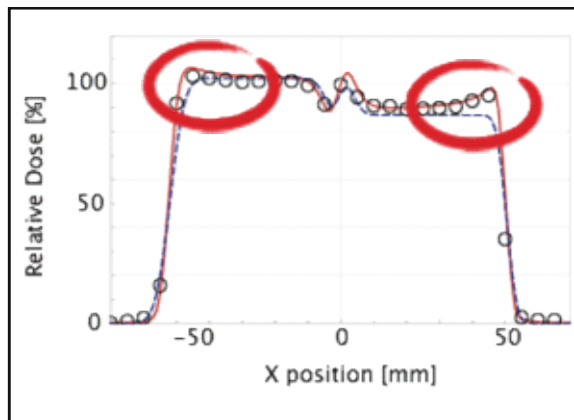
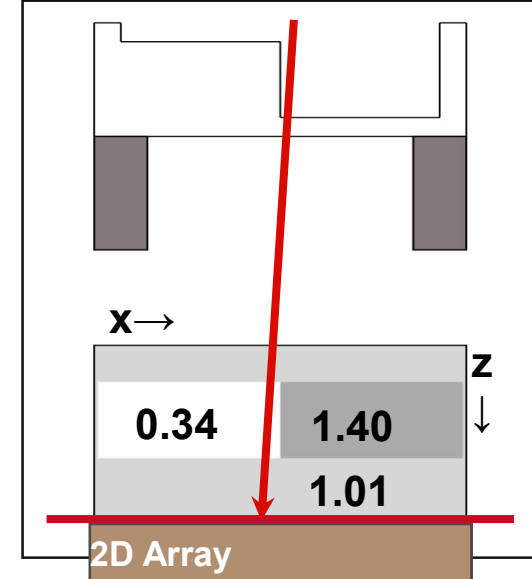
$z = 0$  mm



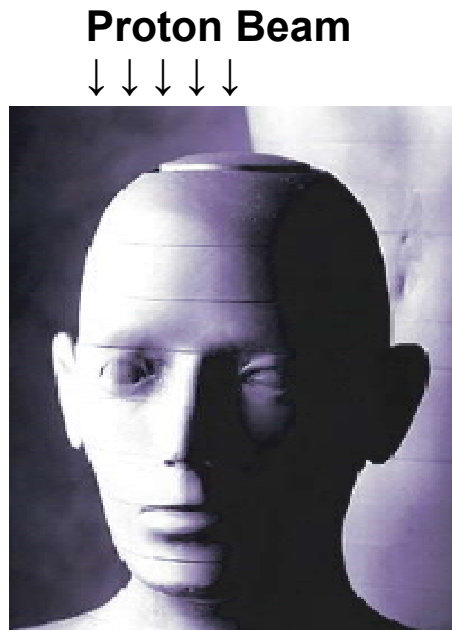
$z = 60$  mm



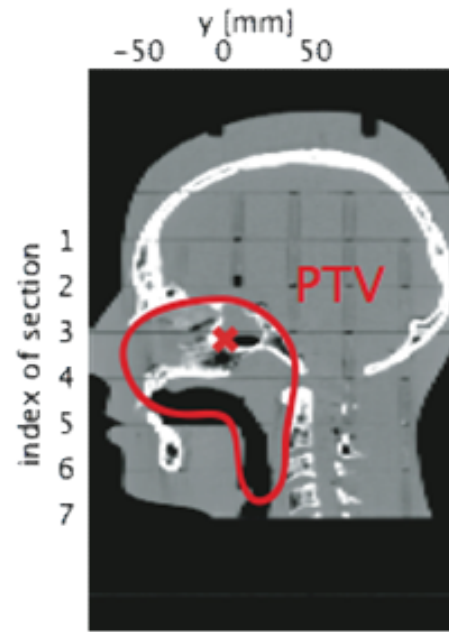
$z = 90$  mm



# Verification in RANDO phantom



Picture



CT

**235 MeV**

**SOBP width 80 mm**

**PTW 2D Array Seven29**

**27 x 27 Matrix (10 mm pitch)**

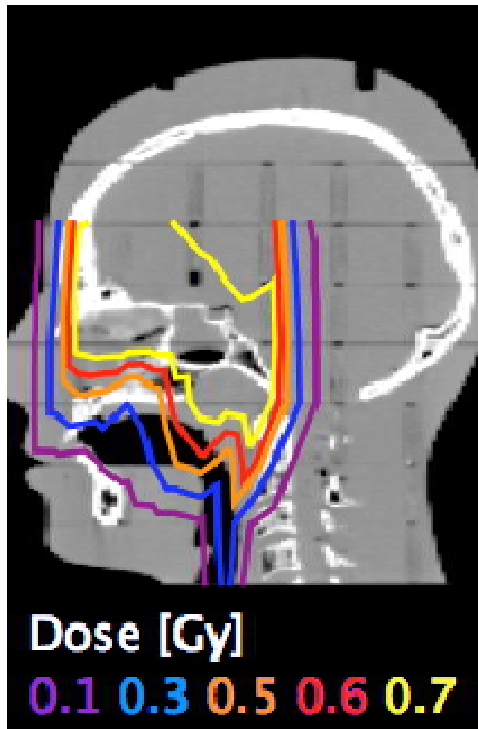
**RANDO Phantom (Head)**

**made by Phantom Laboratory Ltd.**

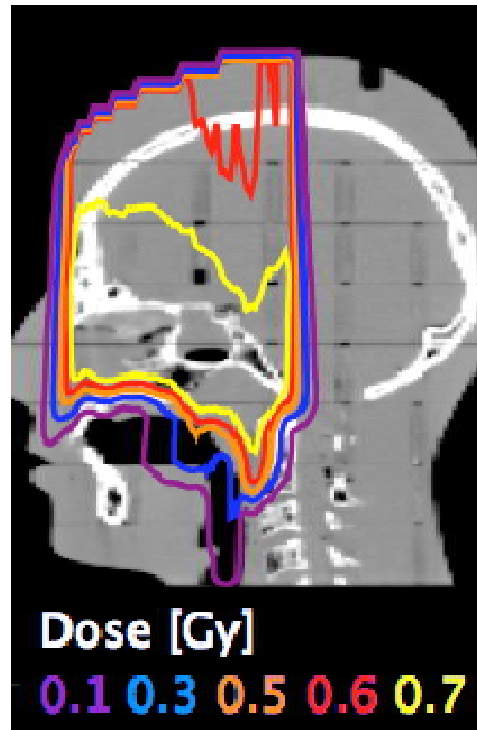
**with section in 25 mm pitch**

# Verification in RANDO phantom

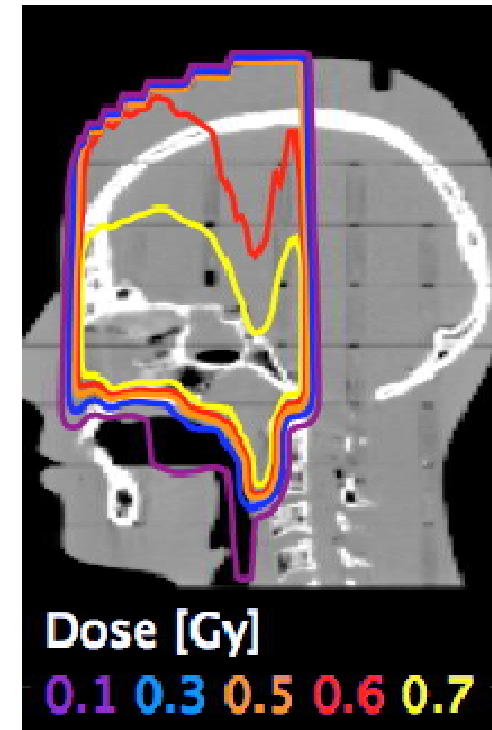
Measurement



SMC (30 min)

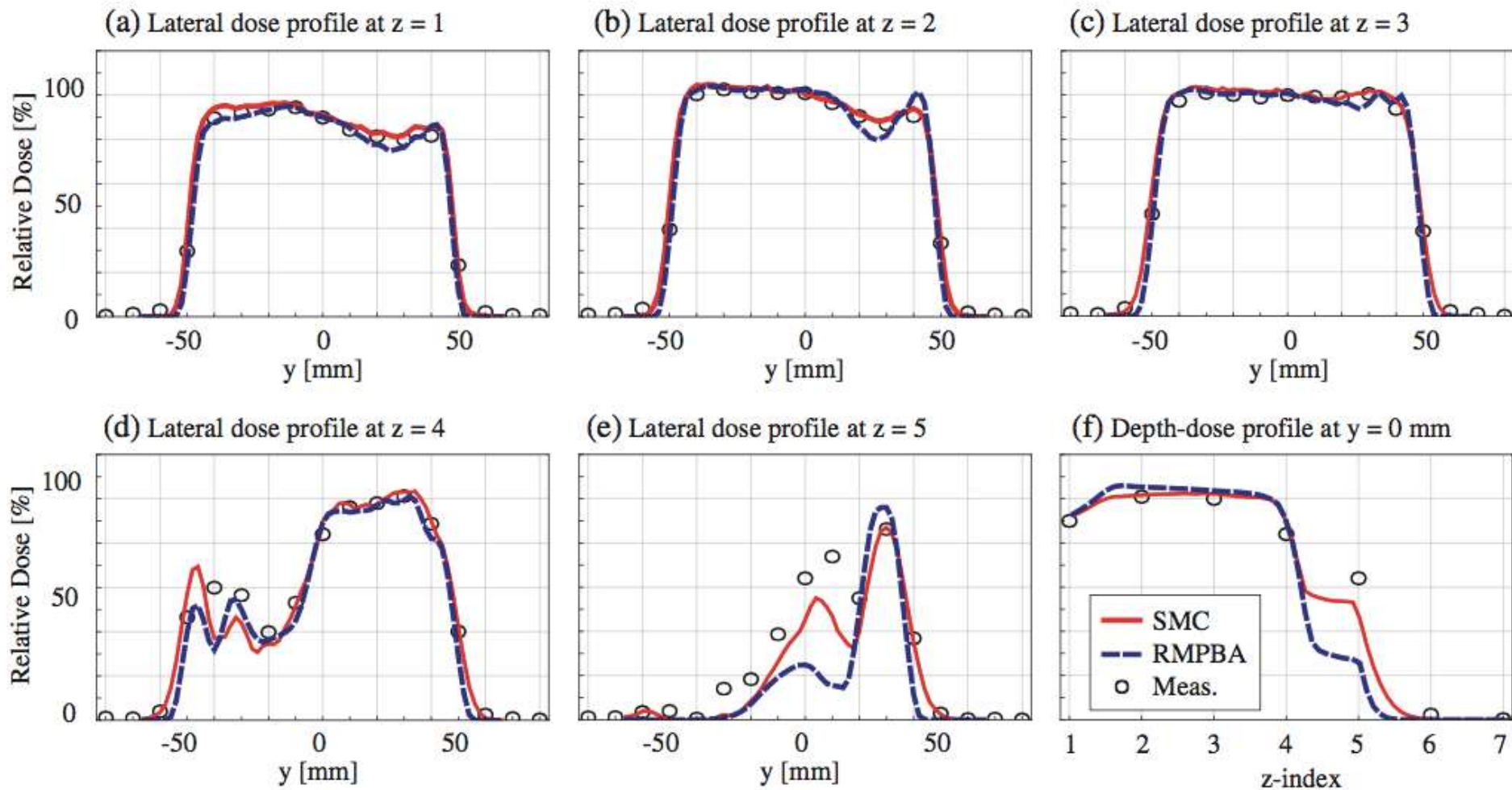


PBA (2 min)



Iso-dose distribution (calculated  
volume = 2.0 liter)

# Verification in RANDO phantom





# Evaluation by gamma index

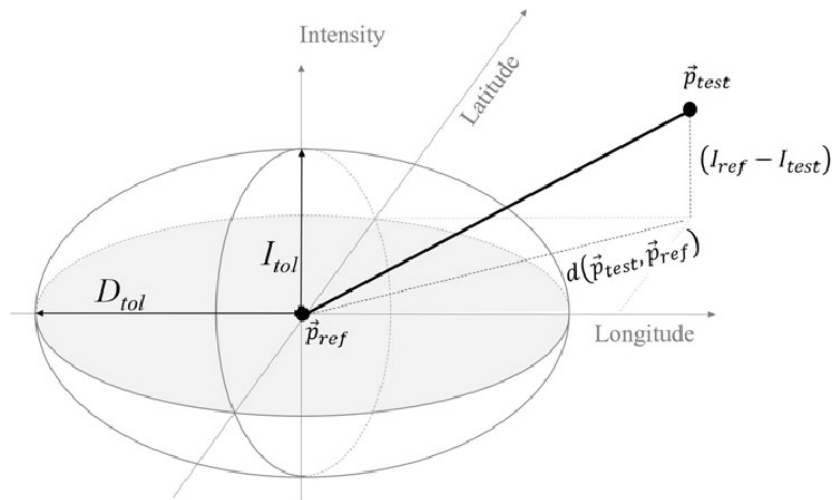
[5] D. A. Low et al; Med. Phys. **25** (1998)

$$\gamma_{\pm}(\mathbf{r}_m) = \min\{|\Gamma(\mathbf{r}_m, \mathbf{r}_c)|\} \forall \{\mathbf{r}_c\}$$

$$\Gamma(\mathbf{r}_m, \mathbf{r}_c) = \sqrt{\frac{|\mathbf{r}_m - \mathbf{r}_c|^2}{\Delta d_M^2 = 3\text{ mm}} + \frac{(D_m(\mathbf{r}_m) - D_c(\mathbf{r}_c))^2}{\Delta D_M^2 = 3\%}}$$

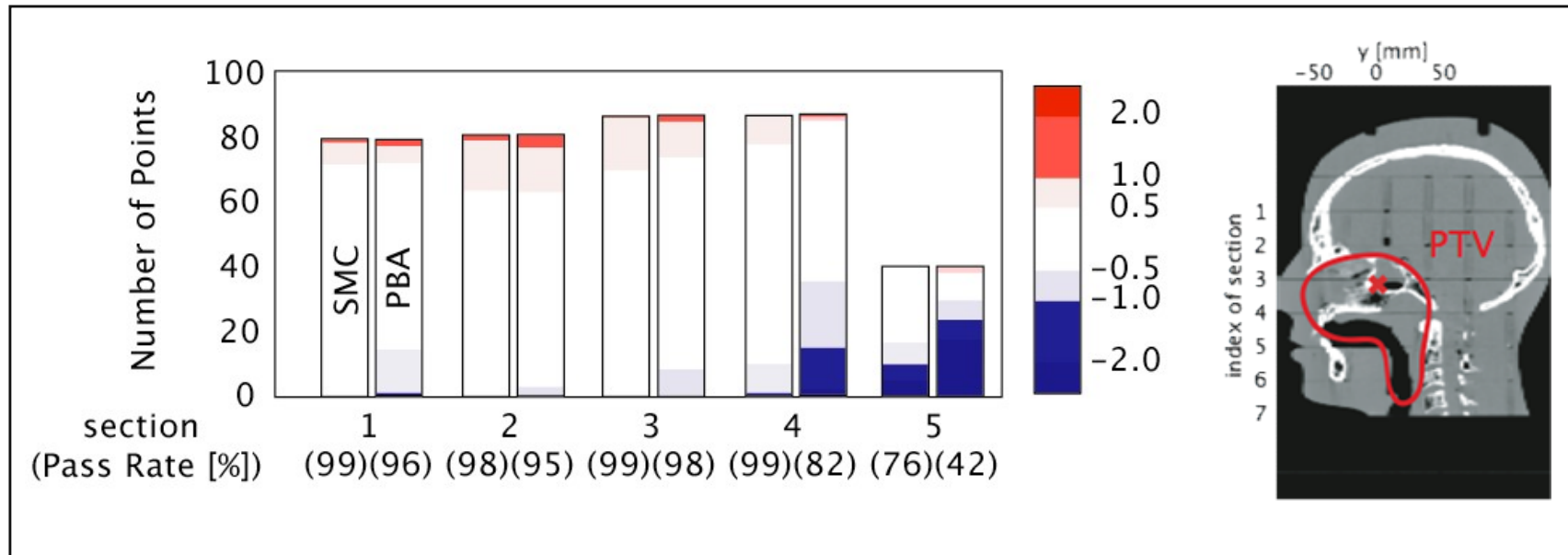
Position error

Dose error



**$D_c$  : calculated dose**  
 **$D_m$  : measured dose**  
 **$DM$  : Tolerance dose error**  
 **$dM$  : Tolerance position error**

# Evaluation by gamma index



**Stacked Bar Chart of  $\gamma_{\pm}$  histogram**

アプリケーション 場所 システム SGI治療計画ソフト2.1 7月26日(金) 21:40 pts

ファイル 画像表示 領域指定 アイソセンター指定 治療計画 結果表示 解析 オプション

治療室: 第2照射室

総線量(処方線量): 70 GyE

一回線量: 2 GyE

CT値水等価厚変換テーブル: 1F-ONE-M.cvt

切削ドリル径: 5

呼吸同期フラグ: OFF

パッチ照射フラグ: OFF

門番号	照射回数	寝台角度	ガントリー角度	アイソセンター番号
1	13	0	280	1
2	12	0	80	1
3	5	0	315	2
4	5	0	45	2

門の追加 門の削除 照射条件追加

門番号: 1

エネルギー

照射タイプ

照射回数

照射総線量

寝台角度

90 270 180

度 280 度

アイソセンター番号: 1

スノート位置: 220 mm

側方マージン: 10 mm

深さマージン: 4 mm

コリメータの種類: 個人用

ボータスの種類: 個人用

スノート干渉チェック

治療部位:  頭頸部  体幹部

ICと寝台の距離: 10.0 mm

ICと寝台境界距離(s-I方向): 10.0 mm

手上げ台サイズ(A-P方向): 10.0 mm

34/78 (21.0) [GyE] 240 73.5 70.0 66.5 63.0 56.0 35.0 14.0 40 -160 34

線量計算

計算デバイス:  CPU  GPU

線量計算手法:  MC-PBA  SMC 粒子数: 10000  SMC\_THEO(G1のみ) ボータス内散乱:  ON  OFF  PBA

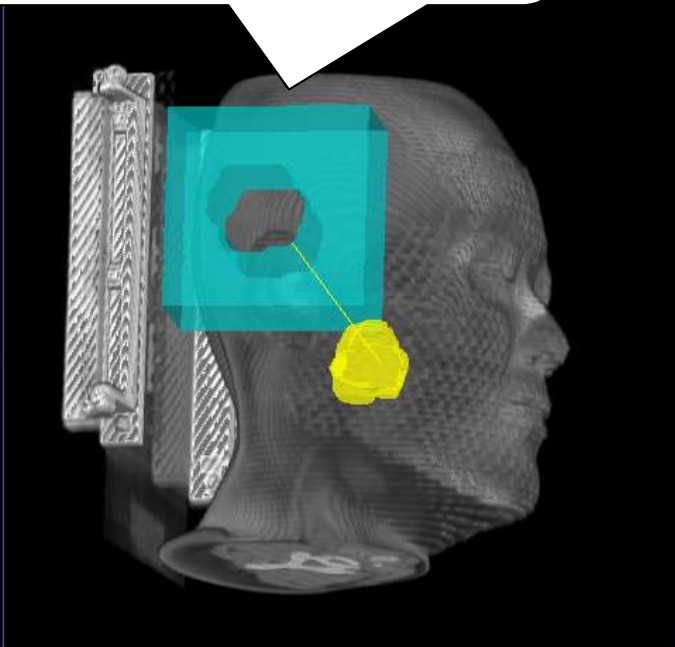
ndose・線量計算共通オプション

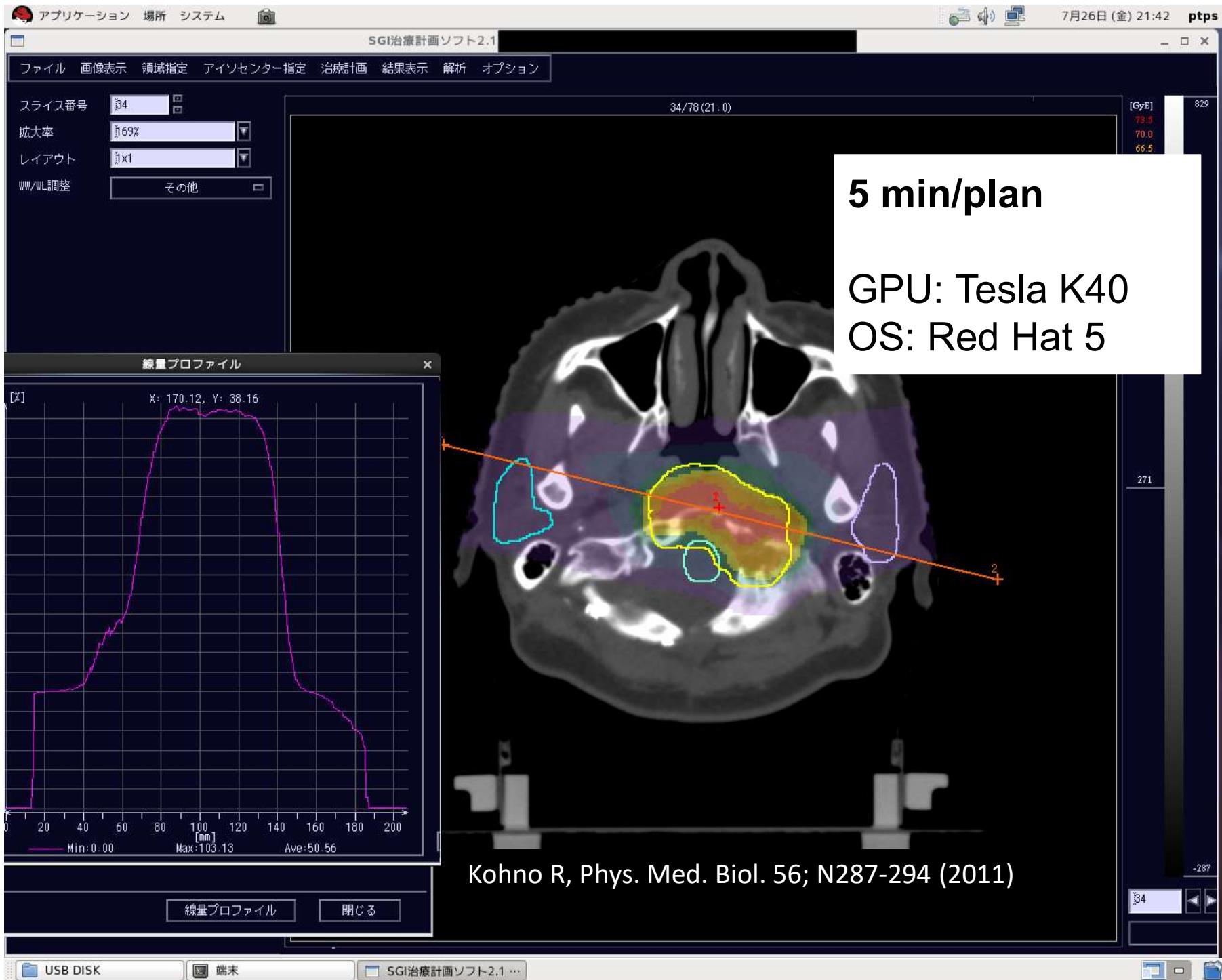
計算範囲:  全スライス  範囲指定: 1 ~ 78

ndoseオプション:  ログ取得設定  取得する  取得しない

USB DISK 端末 SGI治療計画ソフト2.1 ...

To control the statistical error:  
Particle numbers per pixel

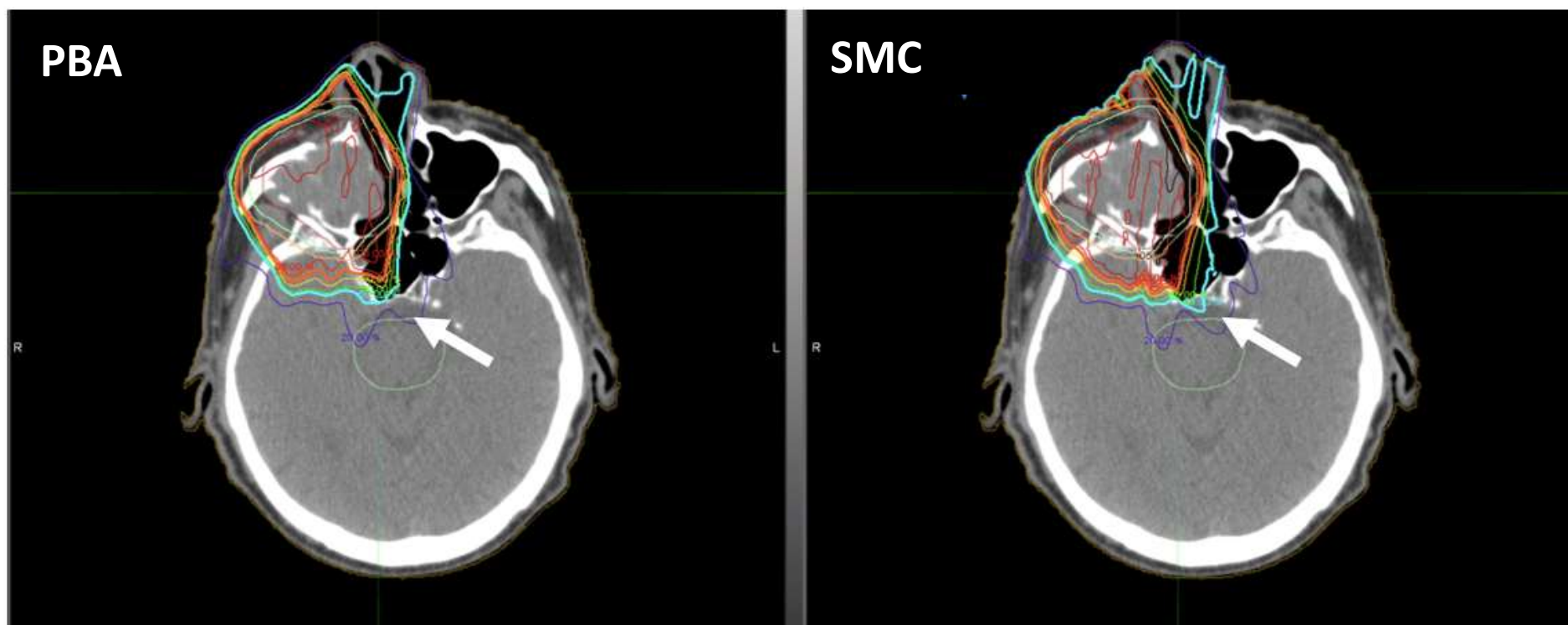




**5 min/plan**  
GPU: Tesla K40  
OS: Red Hat 5

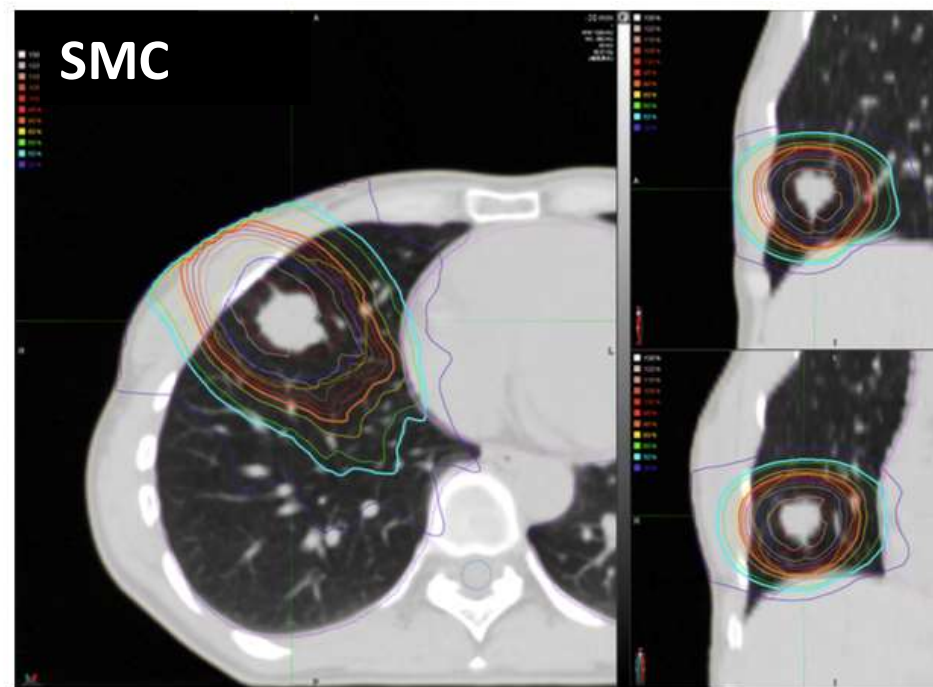
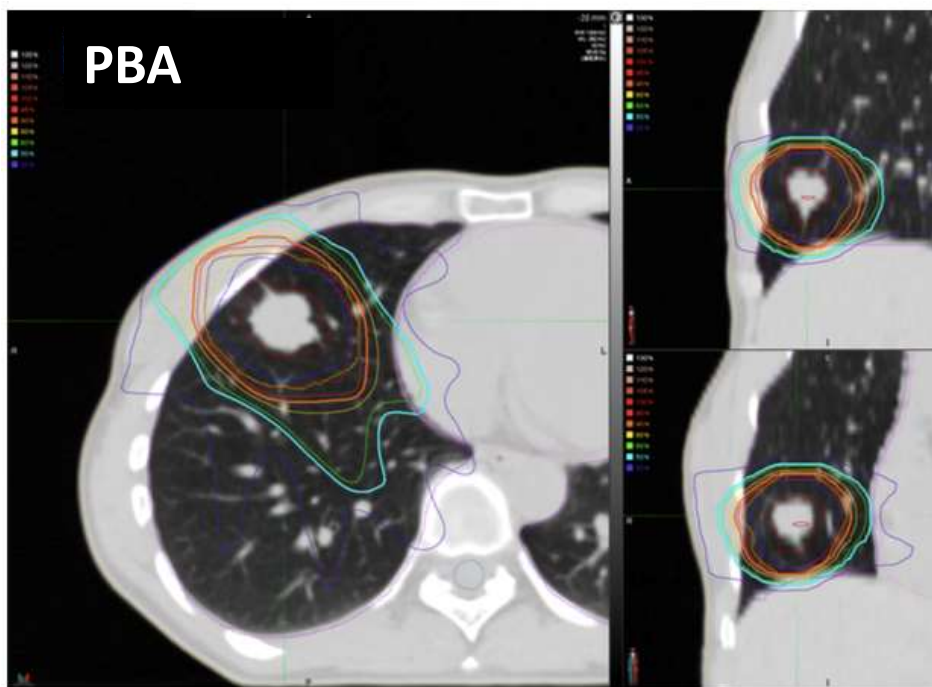
Kohno R, Phys. Med. Biol. 56; N287-294 (2011)

# Change of Dose Distribution





# Change of Dose Distribution





## Discussion to change the TPS



- Dose distribution can be change

Our protocol based on photon RT outcome.

- Absolute dose is not change. (decided by patient calb.)
- Old TPS is going to be broken.

→Now SMC is in clinical use.



# Outlines



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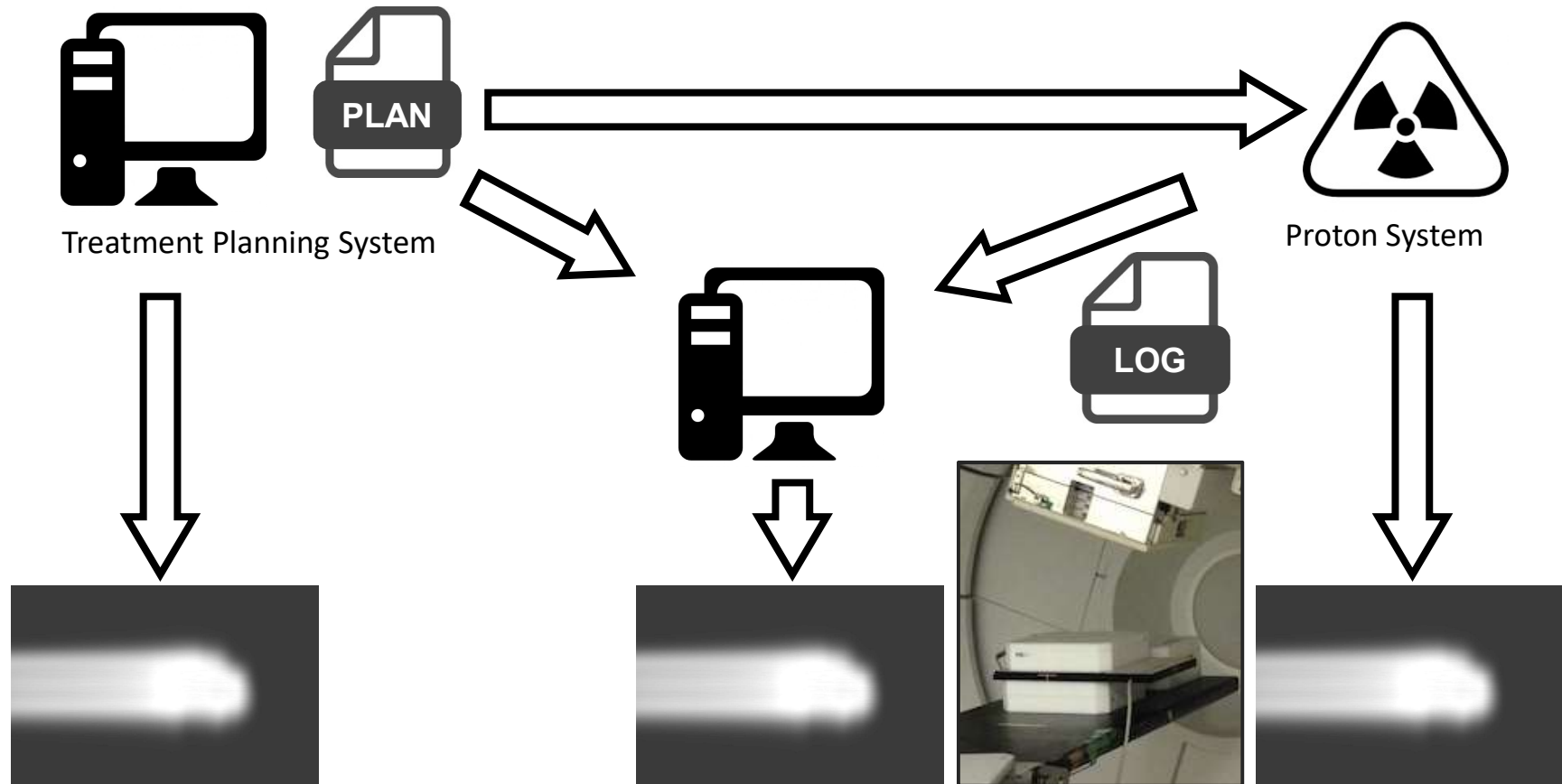
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# Independent Dose Calculation

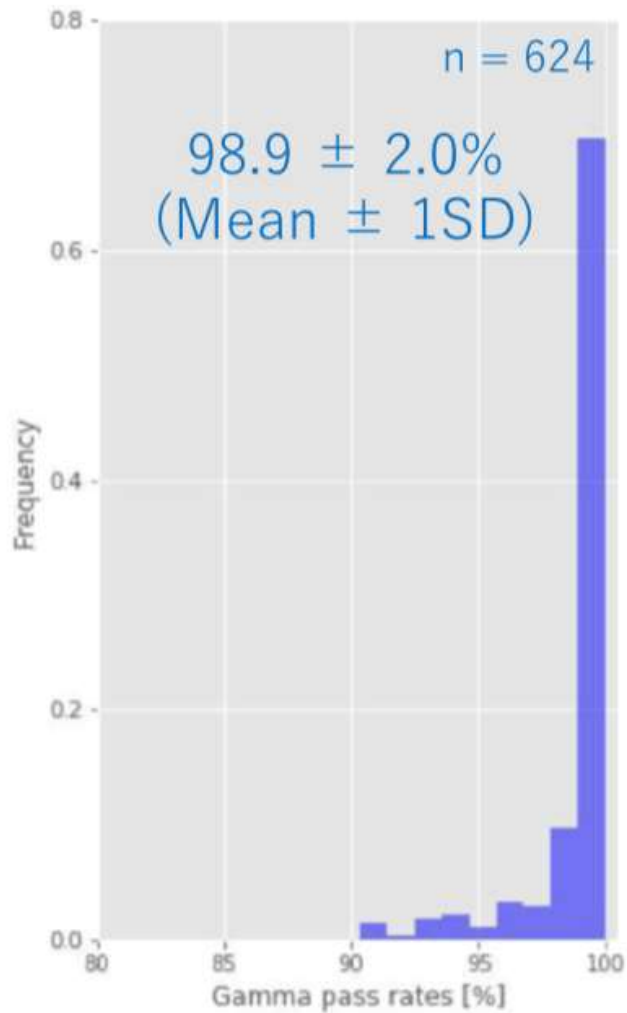
IDC(Independent Dose Calculation system) :

construct the 3D dose distribution from stack of 2D log data

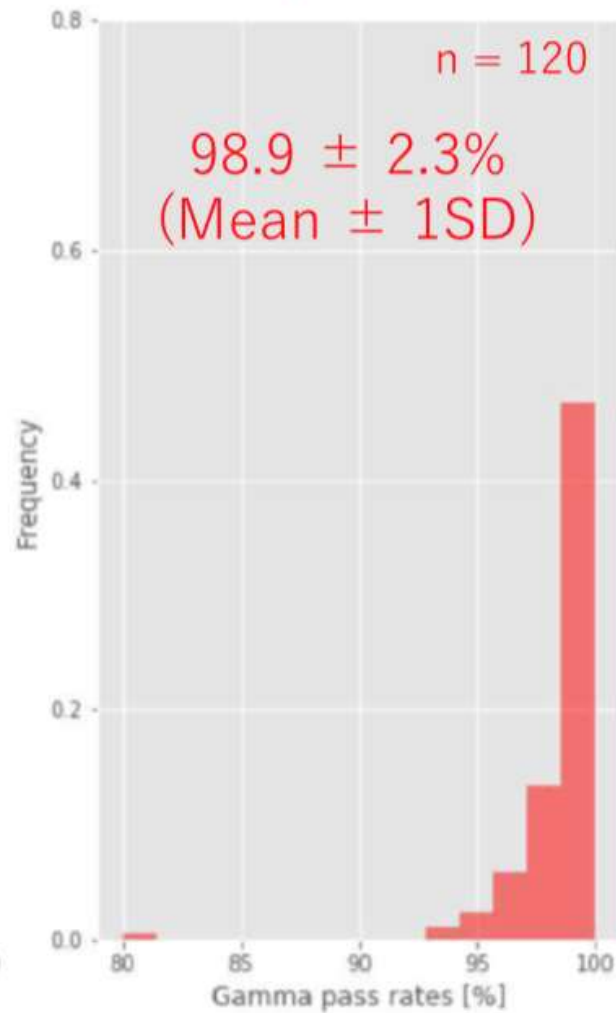


# Independent Dose Calculation

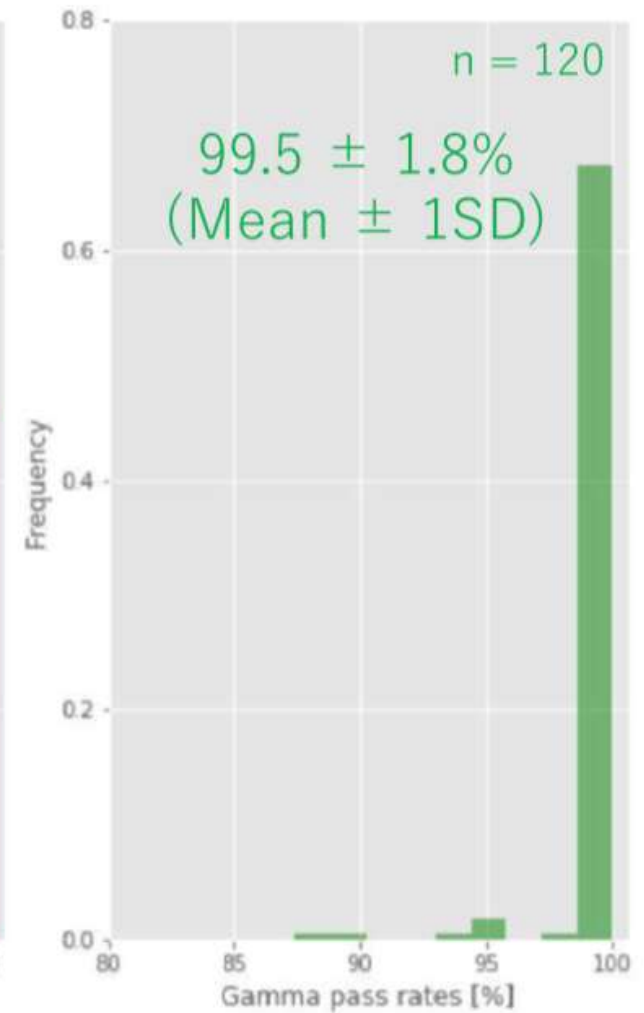
2D-Array vs TPS



2D-Array vs IDC



IDC vs TPS

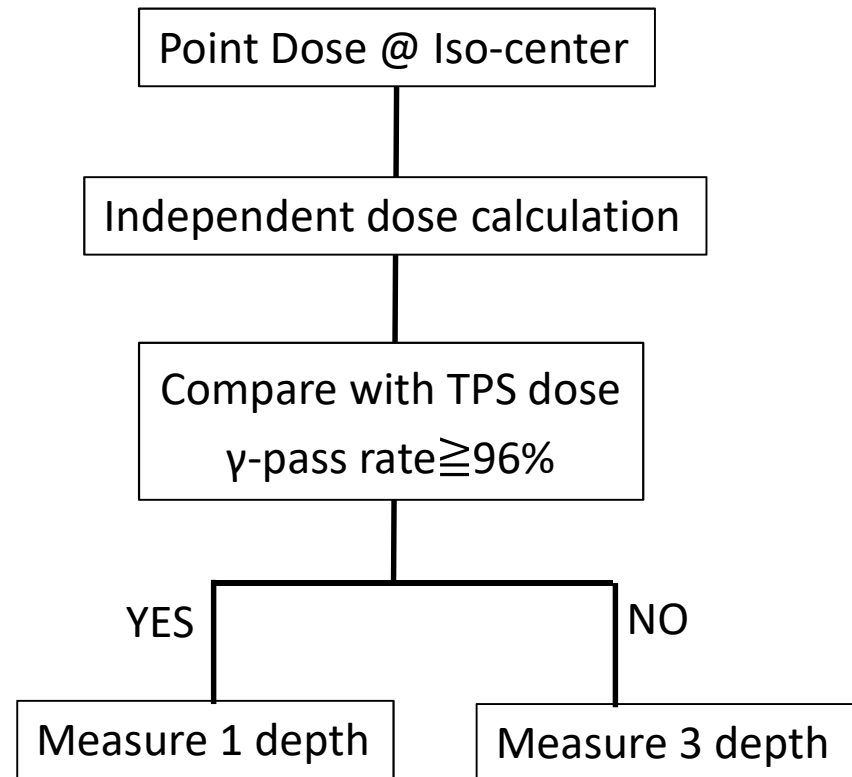


# Independent Dose Calculation (Prostate)

Point Dose @ Iso-center

Tolerance: 1%

Measure 3 depth



QA time: 1 hour → 30 min (/patient)





# Summary



- I introduce hot topics around radiotherapy.
- Now our SMC is being in clinical use.
  - Calculation time is 5 min/plan using GPGPU tech.
  - SMC tends to calculate OAR dose higher than PBA.
- Independent Dose Calculation for Patient QA
  - Reduce the measurement time for Patient QA



**Thank you for your attention.**



# FLASH: ultra high dose rate RT

Science Translational Medicine 16 Jul 2014 Vol. 6, Issue 245, p245

## RESEARCH ARTICLE

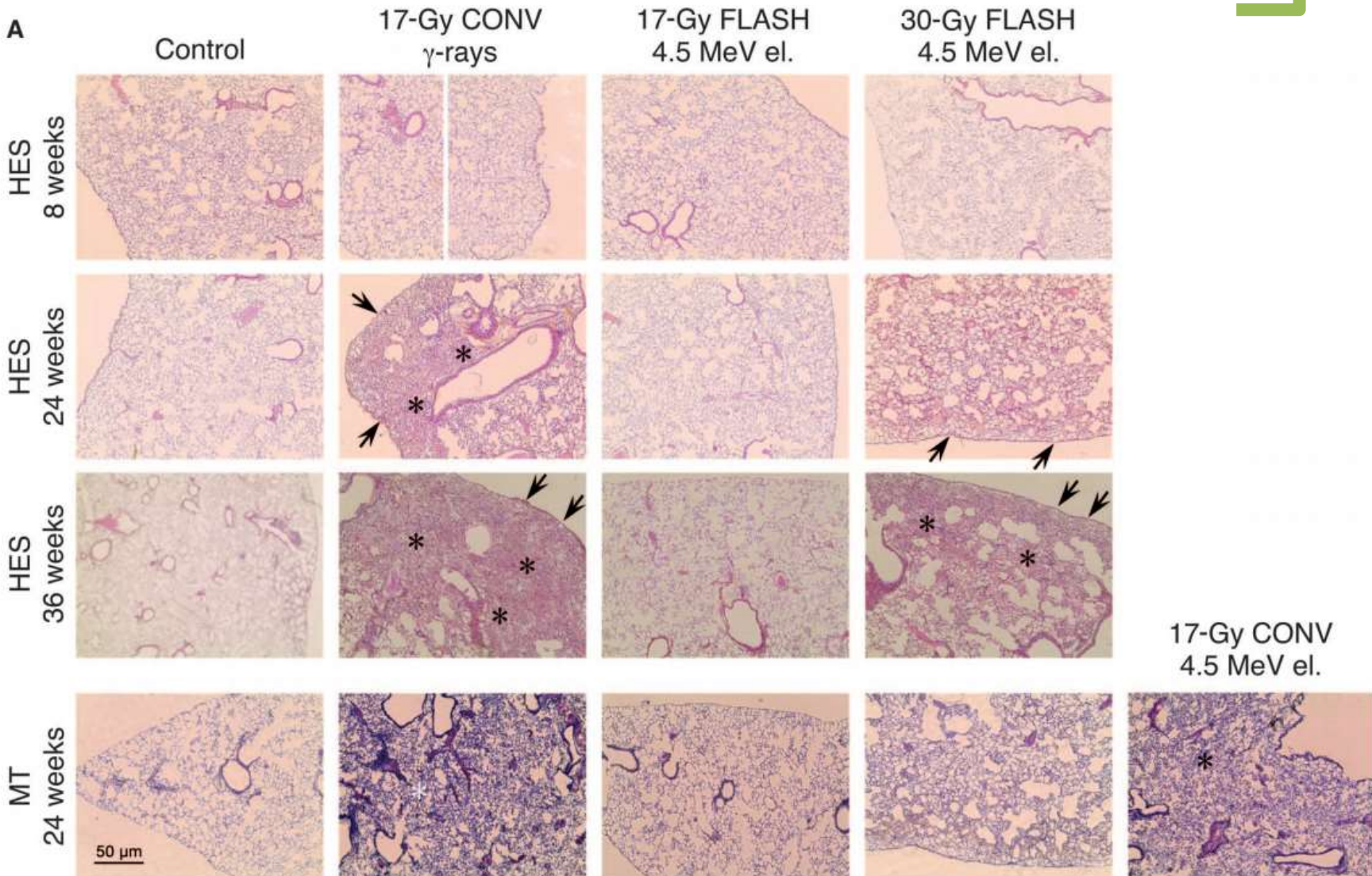
### RADIATION TOXICITY

## Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice

Vincent Favaudon,<sup>1,2\*</sup> Laura Caplier,<sup>3†</sup> Virginie Monceau,<sup>4,5‡</sup> Frédéric Pouzoulet,<sup>1,2§</sup>  
Mano Sayarath,<sup>1,2¶</sup> Charles Fouillade,<sup>1,2</sup> Marie-France Poupon,<sup>1,2||</sup>  
Isabel Brito,<sup>6,7</sup> Philippe Hupé,<sup>6,7,8,9</sup> Jean Bourhis,<sup>4,5,10</sup> Janet Hall,<sup>1,2</sup>  
Jean-Jacques Fontaine,<sup>3</sup> Marie-Catherine Vozenin<sup>4,5,10,11</sup>

In vitro studies suggested that sub-millisecond pulses of radiation elicit less genomic instability than continuous, protracted irradiation at the same total dose. To determine the potential of ultrahigh dose-rate irradiation in radiotherapy, we investigated lung fibrogenesis in C57BL/6J mice exposed either to short pulses ( $\leq 500$  ms) of radiation delivered at ultrahigh dose rate ( $\geq 40$  Gy/s, FLASH) or to conventional dose-rate irradiation ( $\leq 0.03$  Gy/s, CONV) in single doses. The growth of human HBCx-12A and Hep-2 tumor xenografts in nude mice and syngeneic TC-1 Luc<sup>+</sup> orthotopic lung tumors in C57BL/6J mice was monitored under similar radiation conditions. CONV (15 Gy) triggered lung fibrosis associated with activation of the TGF- $\beta$  (transforming growth factor- $\beta$ ) cascade, whereas no complications developed after doses of FLASH below 20 Gy for more than 36 weeks after irradiation. FLASH irradiation also spared normal smooth muscle and epithelial cells from acute radiation-induced apoptosis, which could be reinduced by administration of systemic TNF- $\alpha$  (tumor necrosis factor- $\alpha$ ) before irradiation. In contrast, FLASH was as efficient as CONV in the repression of tumor growth. Together, these results suggest that FLASH radiotherapy might allow complete eradication of lung tumors and reduce the occurrence and severity of early and late complications affecting normal tissue.

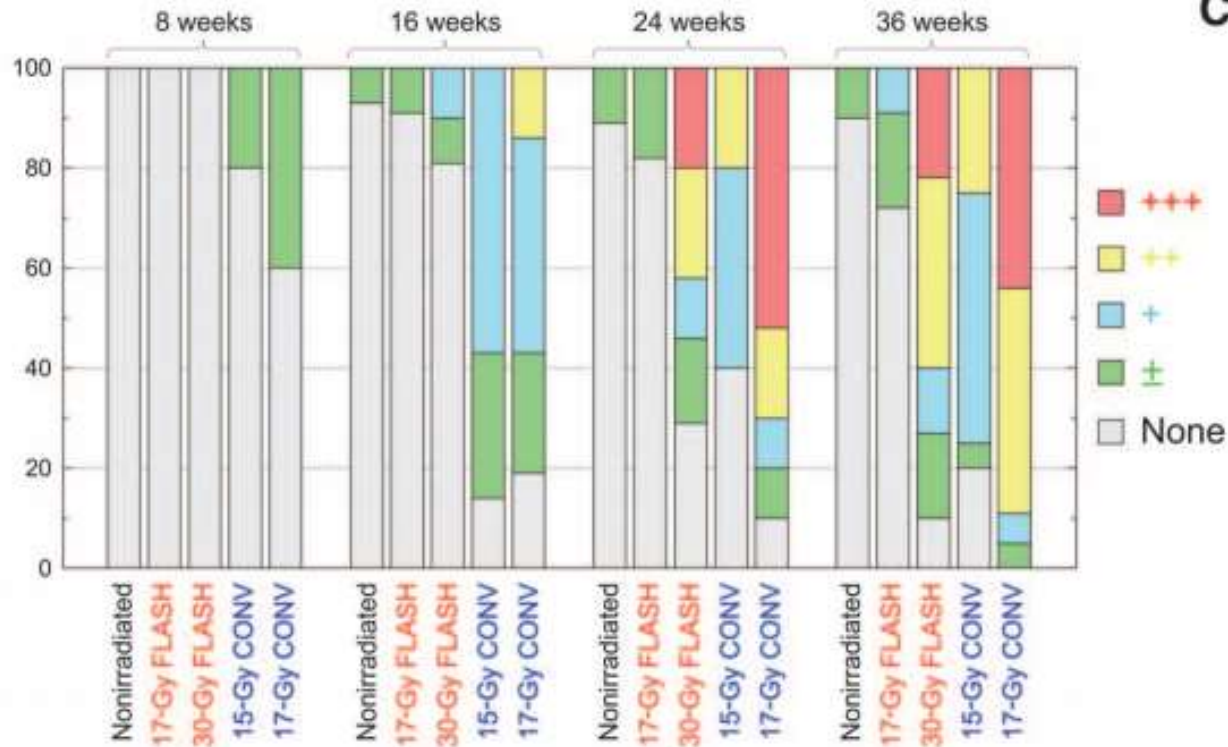
# FLASH: ultra high dose rate RT



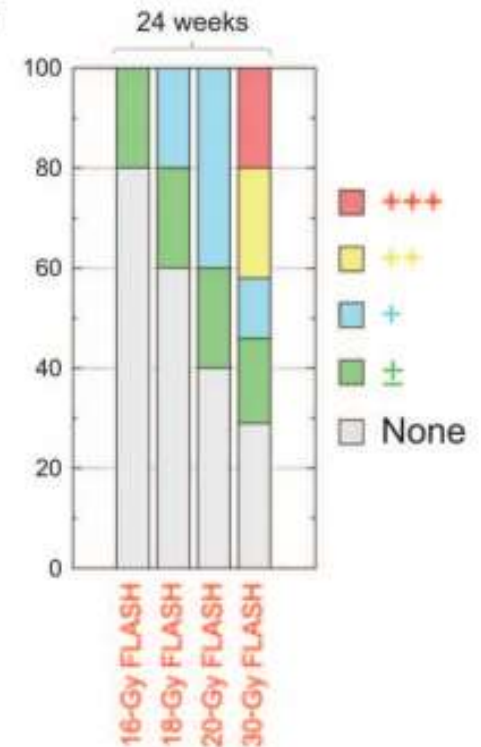


# FLASH: ultra high dose rate RT

**B**

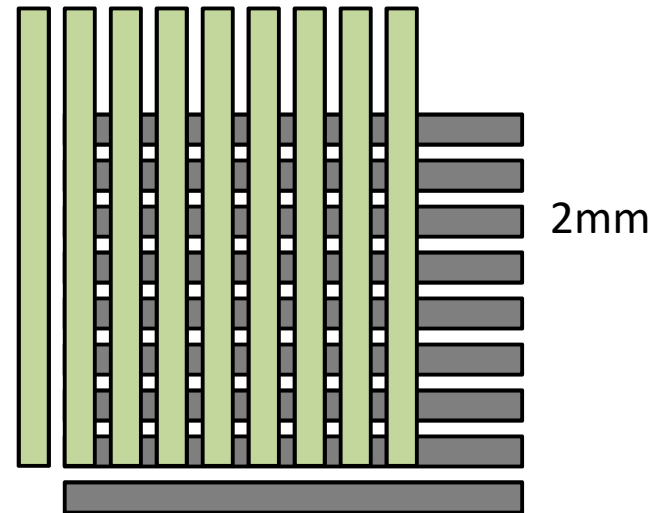


**C**



Lung fibrosis of irradiated mice.

## Measure the beam data with Cross-mini



1-Dimension multi channel detector(101+101)

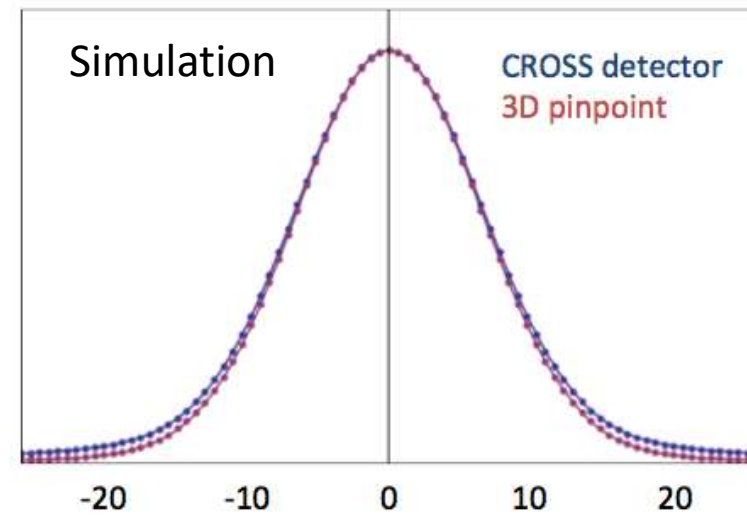
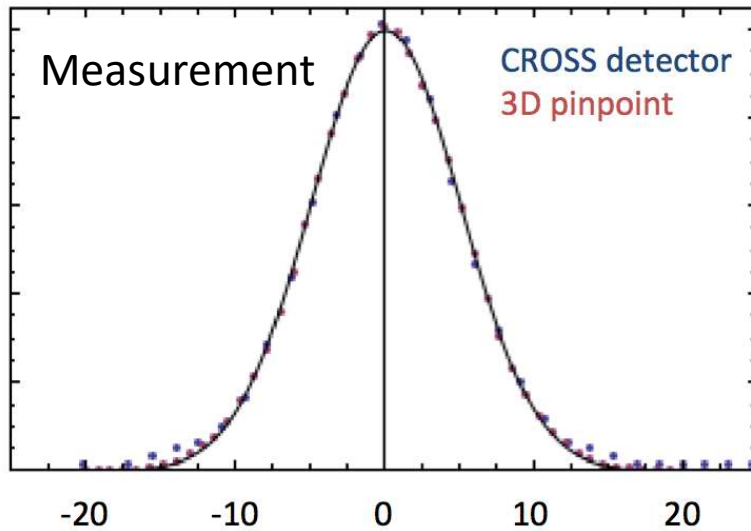
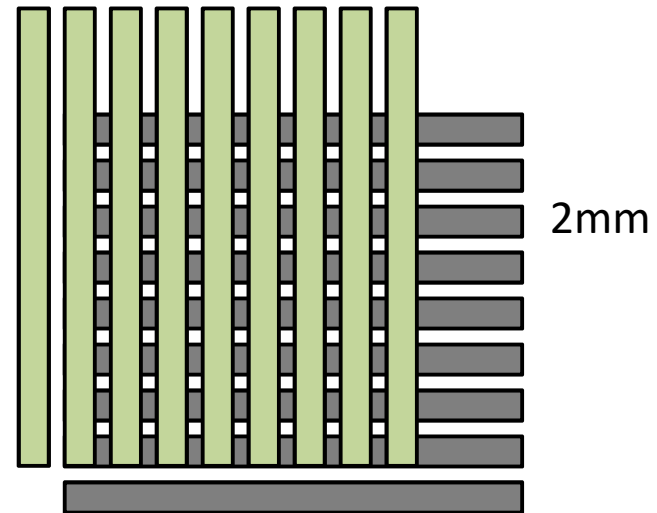
2 mm × 200 mm Parallel plate ionization chamber

- Shorten the measurement time
- Robust to the beam positioning Error
- !!Need to Convert the measurement result

(Because of the detector shape)



# Measure the beam data with Cross-mini



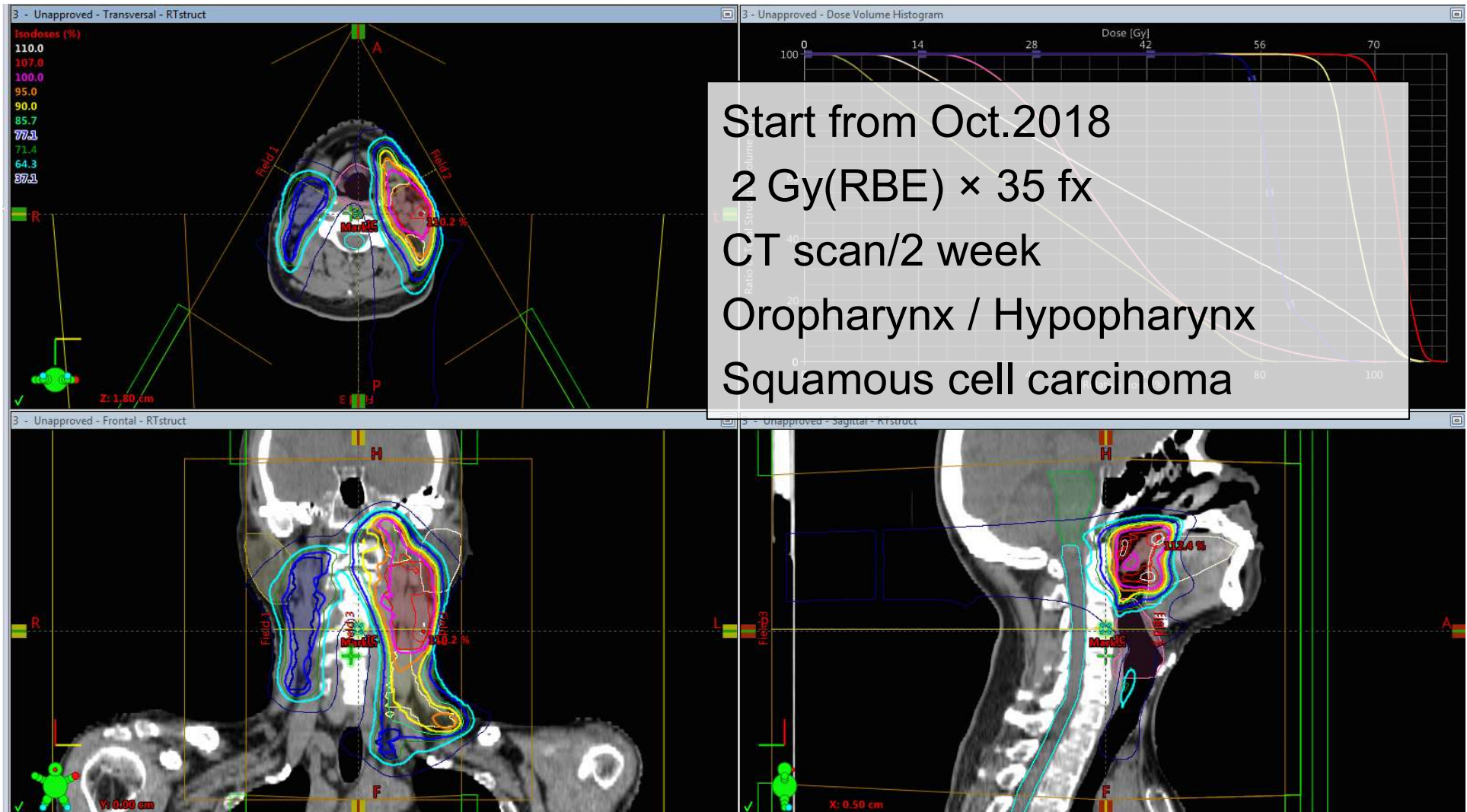
## Measure the beam data with Cross-mini

$$\begin{aligned}\phi(x, y) &= (1 - w) \left( \frac{1}{\sqrt{2\pi}\sigma_{1,x}} \text{Exp}[-2\sigma_{1,x}^2] \cdot \frac{1}{\sqrt{2\pi}\sigma_{1,y}} \text{Exp}[-2\sigma_{1,y}^2] \right) + w \left( \frac{1}{\sqrt{2\pi}\sigma_{2,x}} \text{Exp}[-2\sigma_{2,x}^2] \cdot \frac{1}{\sqrt{2\pi}\sigma_{2,y}} \text{Exp}[-2\sigma_{2,y}^2] \right) \\ \phi_{3DPP}(x) &= \phi(x, y = 0) = (1 - w) \left( \frac{1}{\sqrt{2\pi}\sigma_{1,x}} \text{Exp}[-2\sigma_{1,x}^2] \cdot \frac{1}{\sqrt{2\pi}\sigma_{1,y}} \right) + w \left( \frac{1}{\sqrt{2\pi}\sigma_{2,x}} \text{Exp}[-2\sigma_{2,x}^2] \cdot \frac{1}{\sqrt{2\pi}\sigma_{2,y}} \right) \\ \phi_{Cross}(x) &= \int \phi(x, y) dy = (1 - w) \left( \frac{1}{\sqrt{2\pi}\sigma_{1,x}} \text{Exp}[-2\sigma_{1,x}^2] \right) + w \left( \frac{1}{\sqrt{2\pi}\sigma_{2,x}} \text{Exp}[-2\sigma_{2,x}^2] \right) \\ &= \left( (1 - w) \left( \frac{1}{\sqrt{2\pi}\sigma_{1,x}} \text{Exp}[-2\sigma_{1,x}^2] \cdot \frac{1}{\sqrt{2\pi}\sigma_{1,y}} \right) + \frac{\sqrt{2\pi}\sigma_{2,y}}{\sqrt{2\pi}\sigma_{1,y}} w \left( \frac{1}{\sqrt{2\pi}\sigma_{2,x}} \text{Exp}[-2\sigma_{2,x}^2] \cdot \frac{1}{\sqrt{2\pi}\sigma_{2,y}} \right) \right) \sqrt{2\pi}\sigma_{1,y}\end{aligned}$$

- Shorten the measurement time
- Robust to the beam positioning Error
- !!Need to Convert the measurement result

(Because of the detector shape)

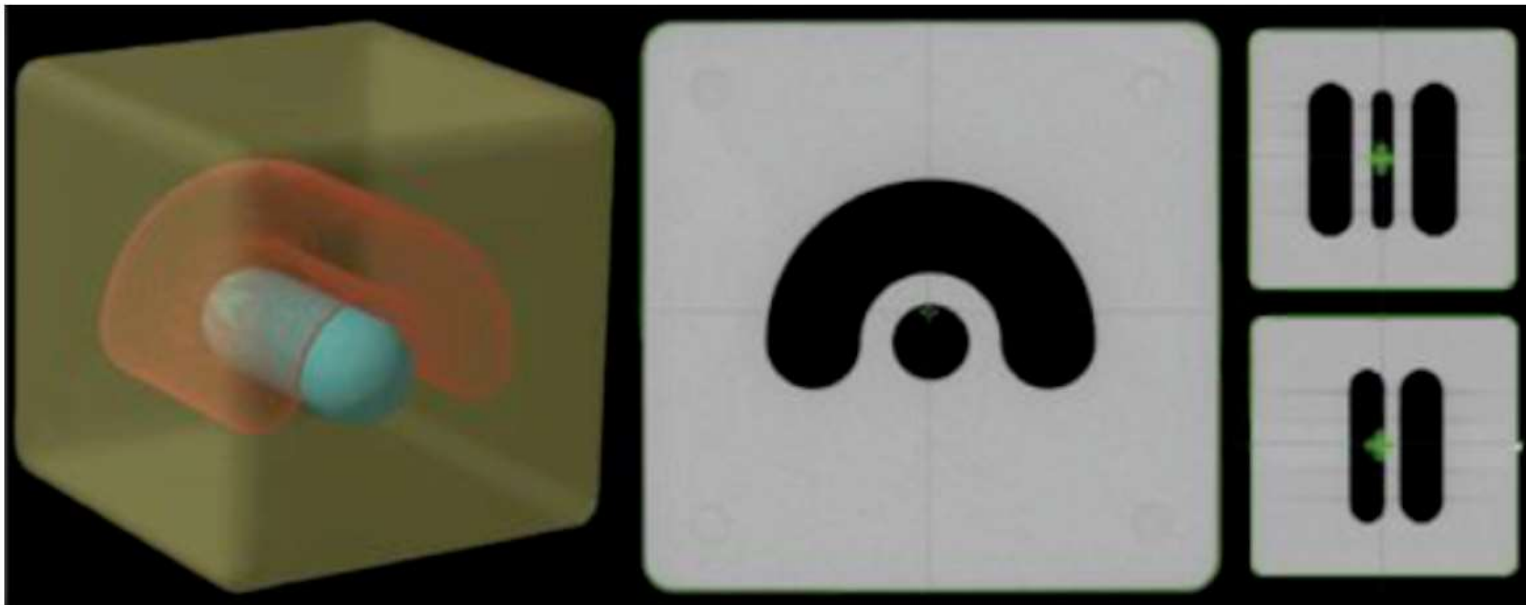
# IMPT for Head & Neck



# H&N IMPT : QA for multi-center study

## Materials

- IMRT Phantom of JCOG(Japan clinical oncology group)
- Film · · · Gafchromic Film(EBT3)
- Chamber · · · PTW30013
- Electrometer · · · UNIDOS webline Universal dosemeter
- Analyze software · · · Simple IMRT Analysis



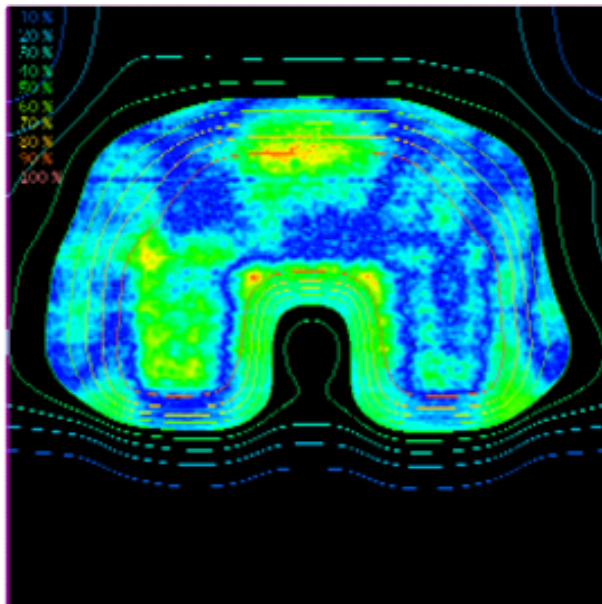
# H&N IMPT : QA for multi-center study

Dose@Iso-center

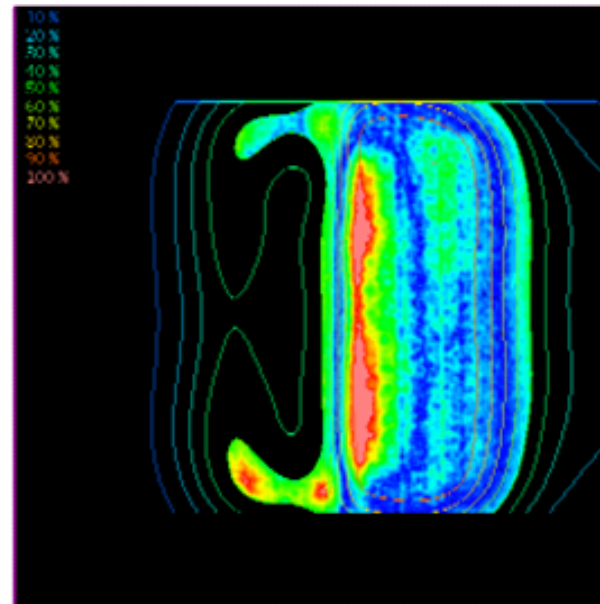
TPS: 1.875 Gy    Measure : 1.887 Gy    Difference : 0.7%

Dose Distribution  $\gamma$ -pass(3mm/5%)

Axial : 100%

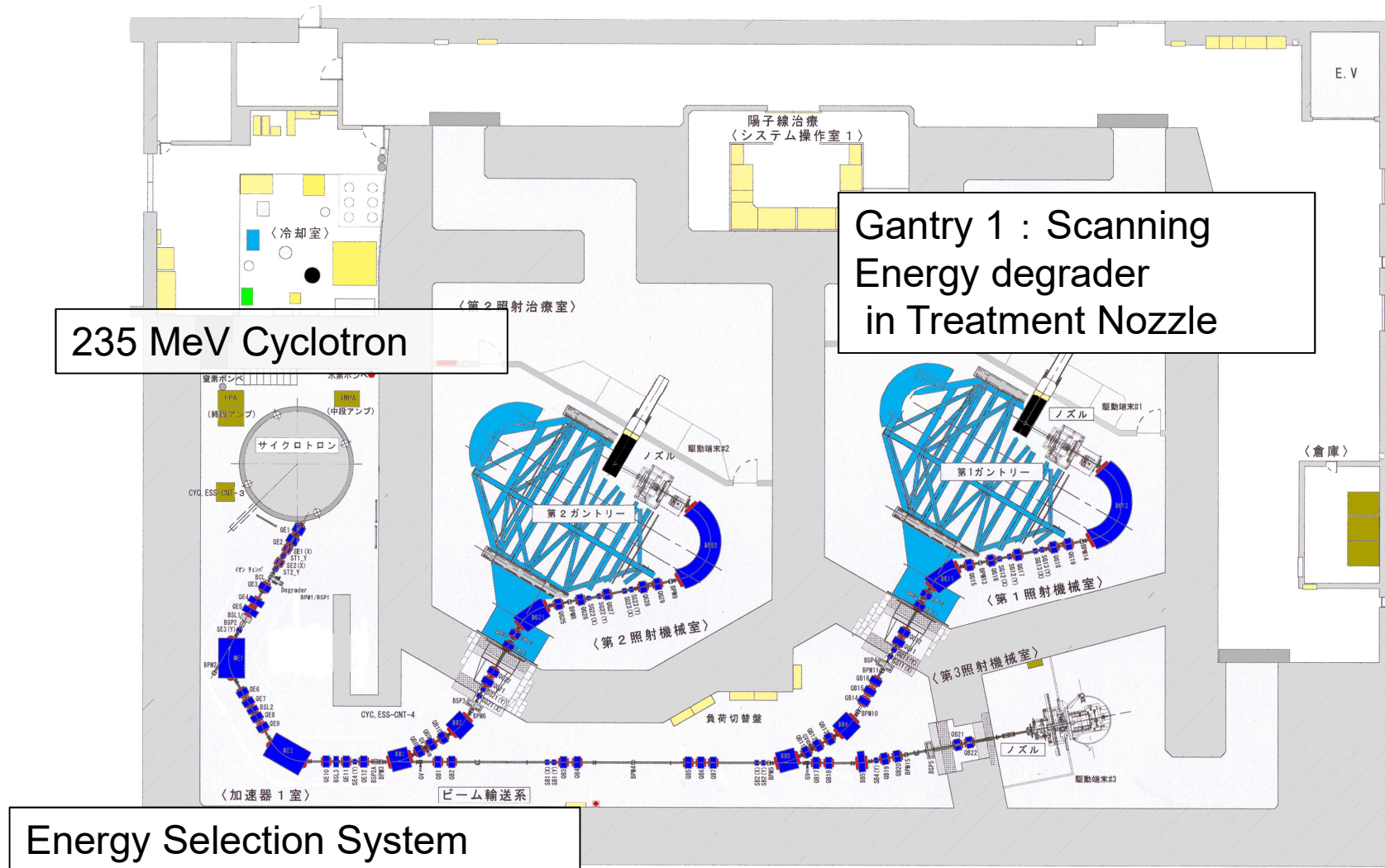


Sagittal : 96.9%

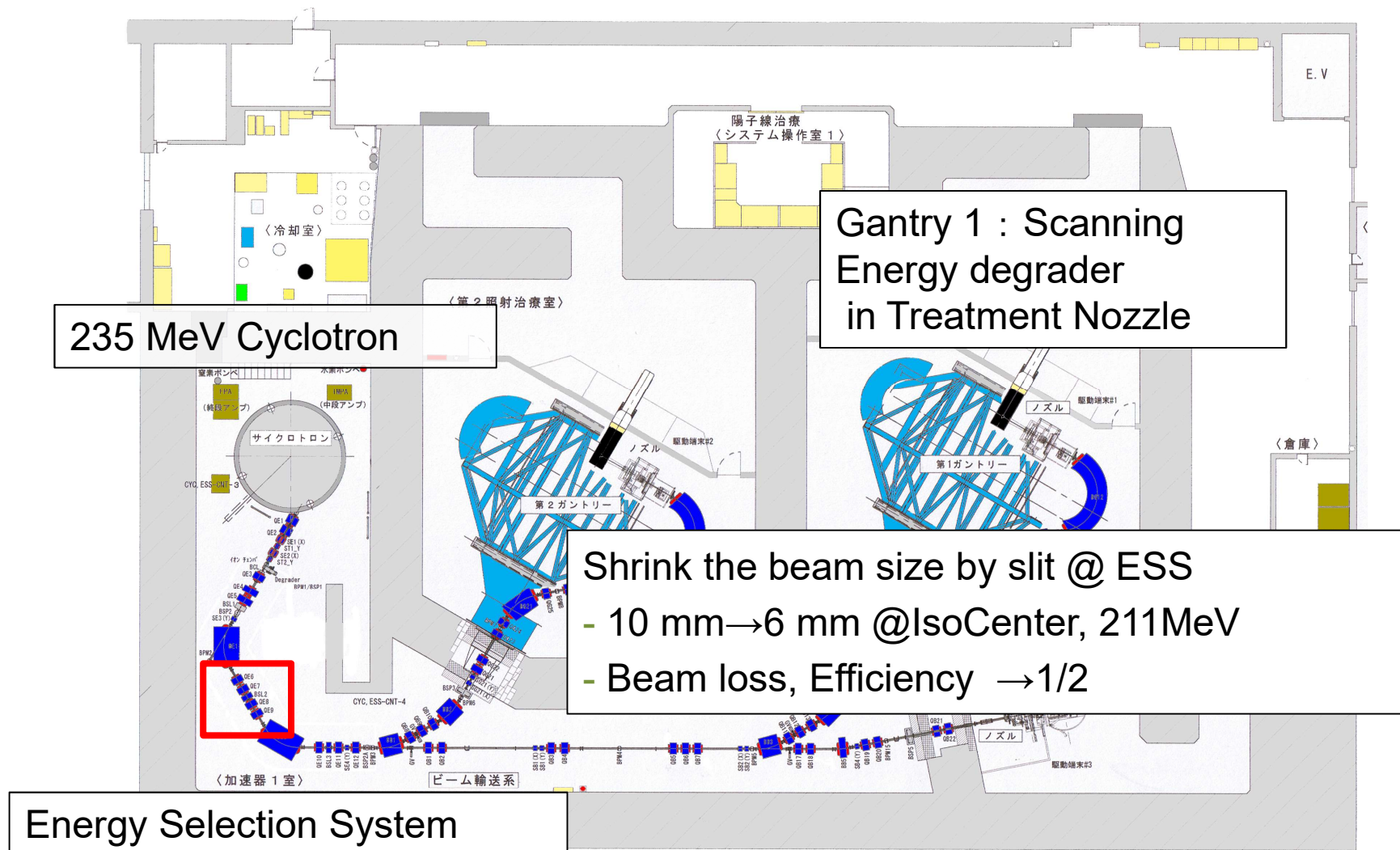




# Proton Therapy System (Scanning)



# Shrink the beam size



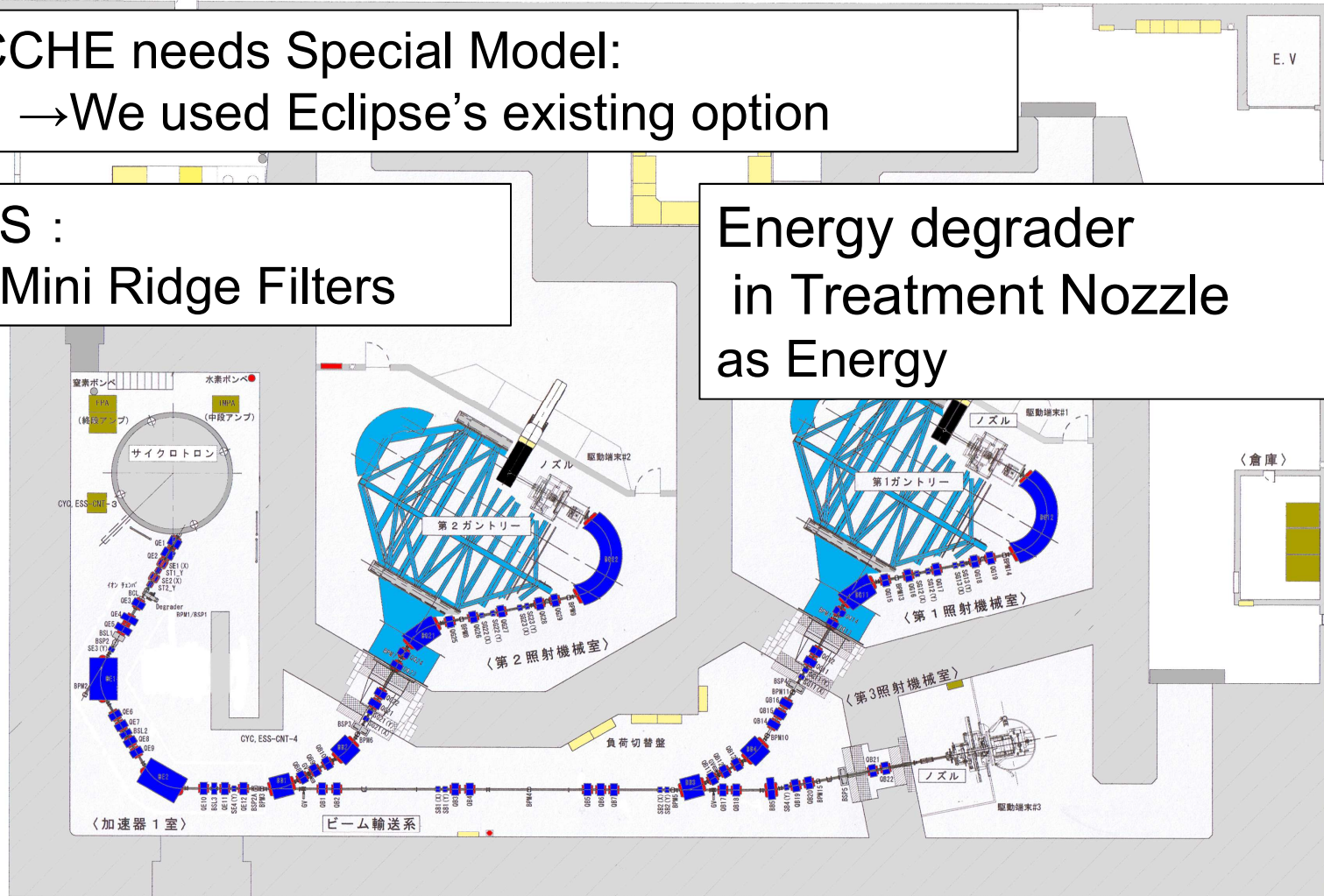


# Change the TPS : Eclipse

NCCHE needs Special Model:  
→We used Eclipse's existing option

ESS :  
as Mini Ridge Filters

Energy degrader  
in Treatment Nozzle  
as Energy





# Outlines



## Introduction of Our Unique Approaches

- About National Cancer Center Hospital East
- Works to Realize Intensity Modulation Proton Therapy
- **Use of Cross-mini: Chamber Array**
- Independent Dose Calculation for Patient QA



# Outlines



## Introduction of Our Unique Approaches

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