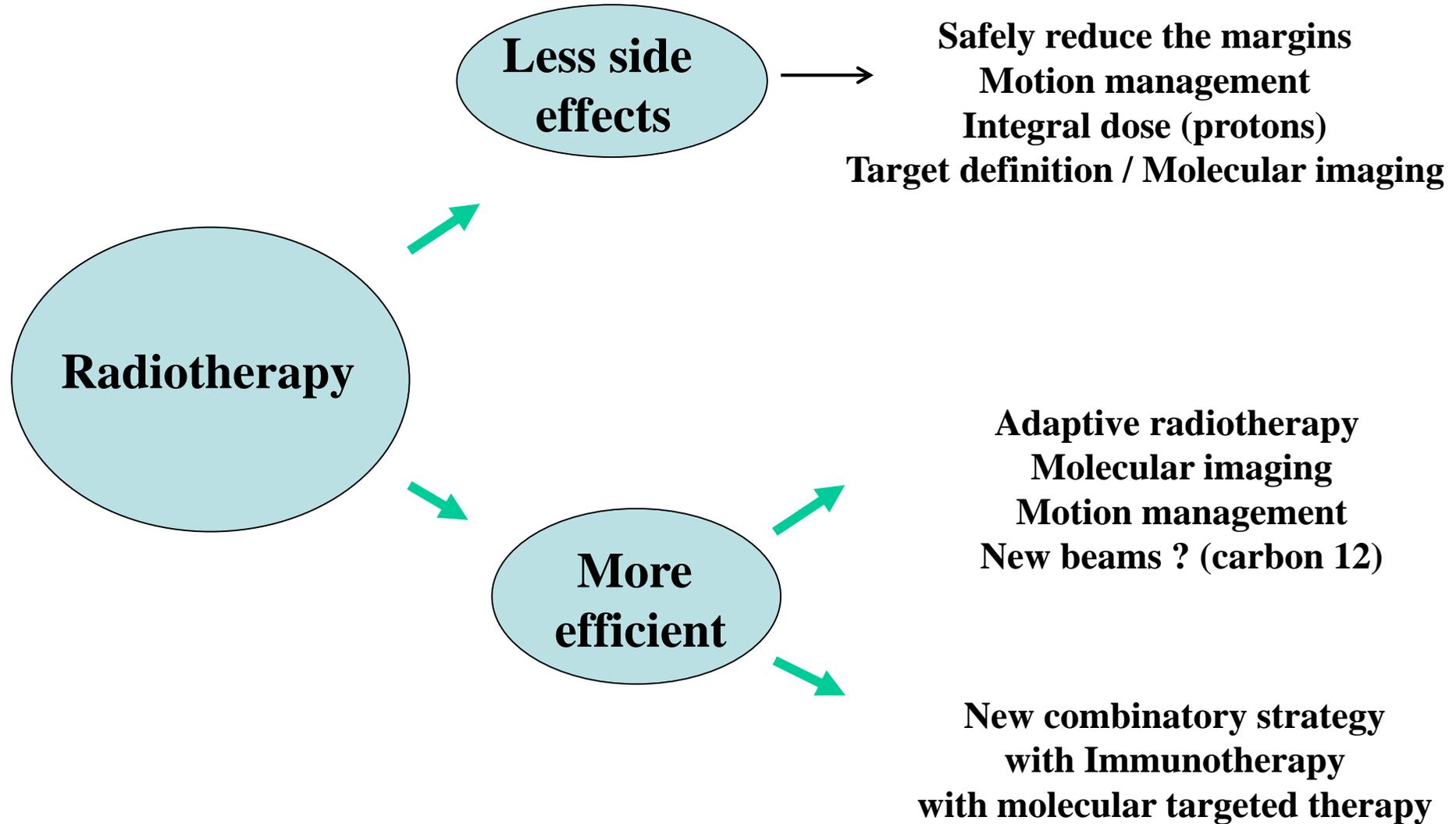


# Towards new types of irradiation ?

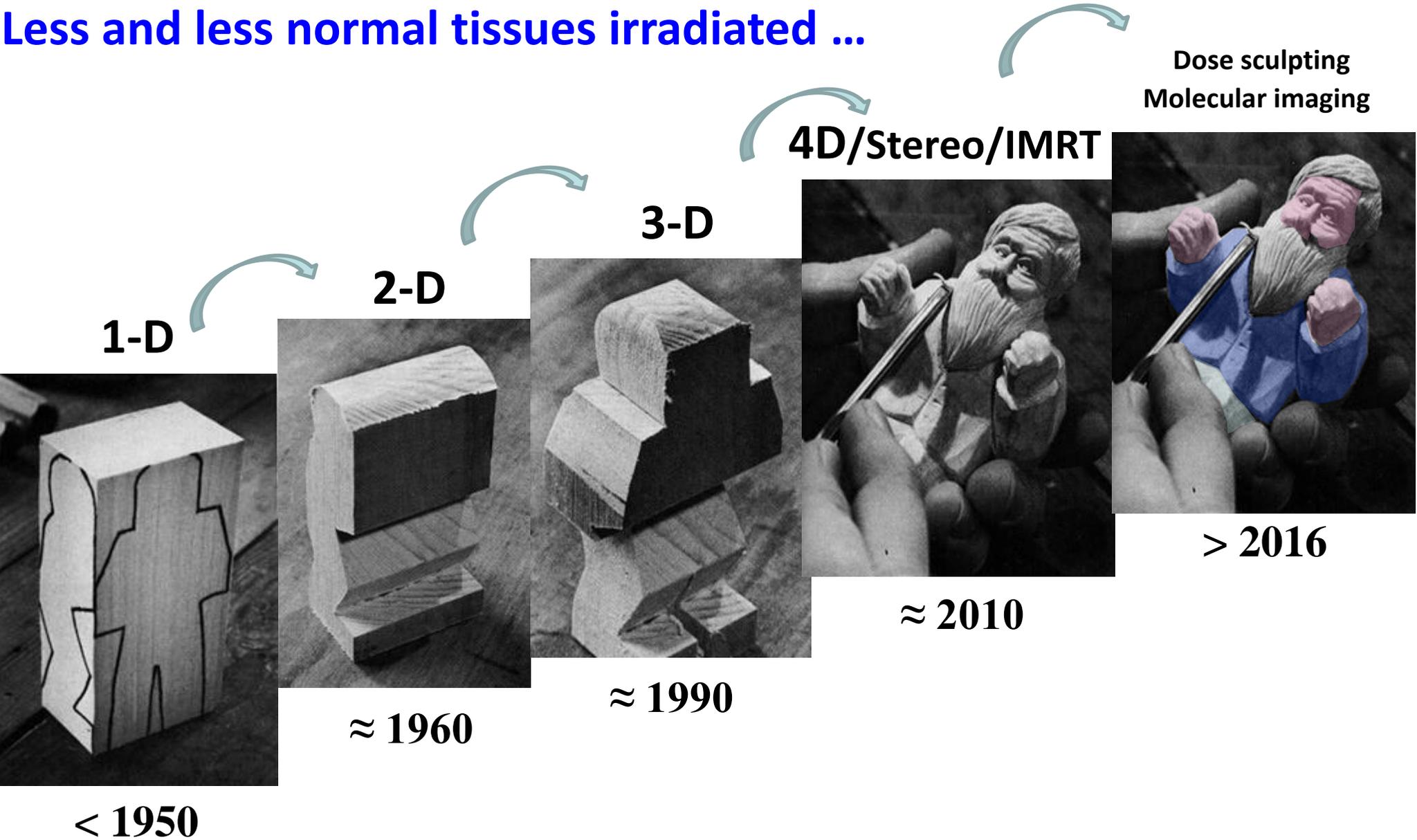
J Bourhis, MC Vozenin, N Peguret, M Ozsahin, R Moeckli, M Jaccard, JF Germond

Swiss Cancer Center Lausanne

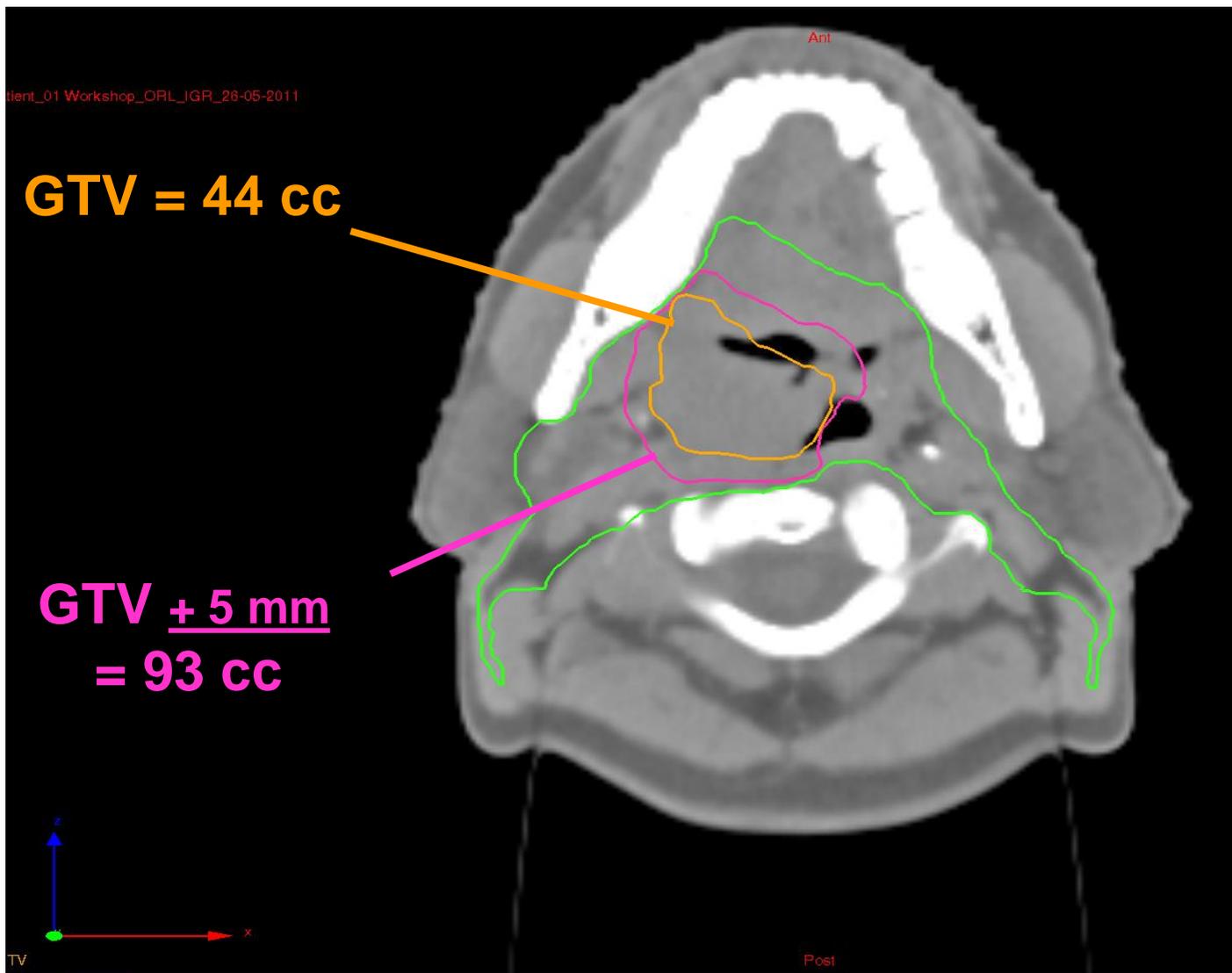
# How to improve radiotherapy ?...



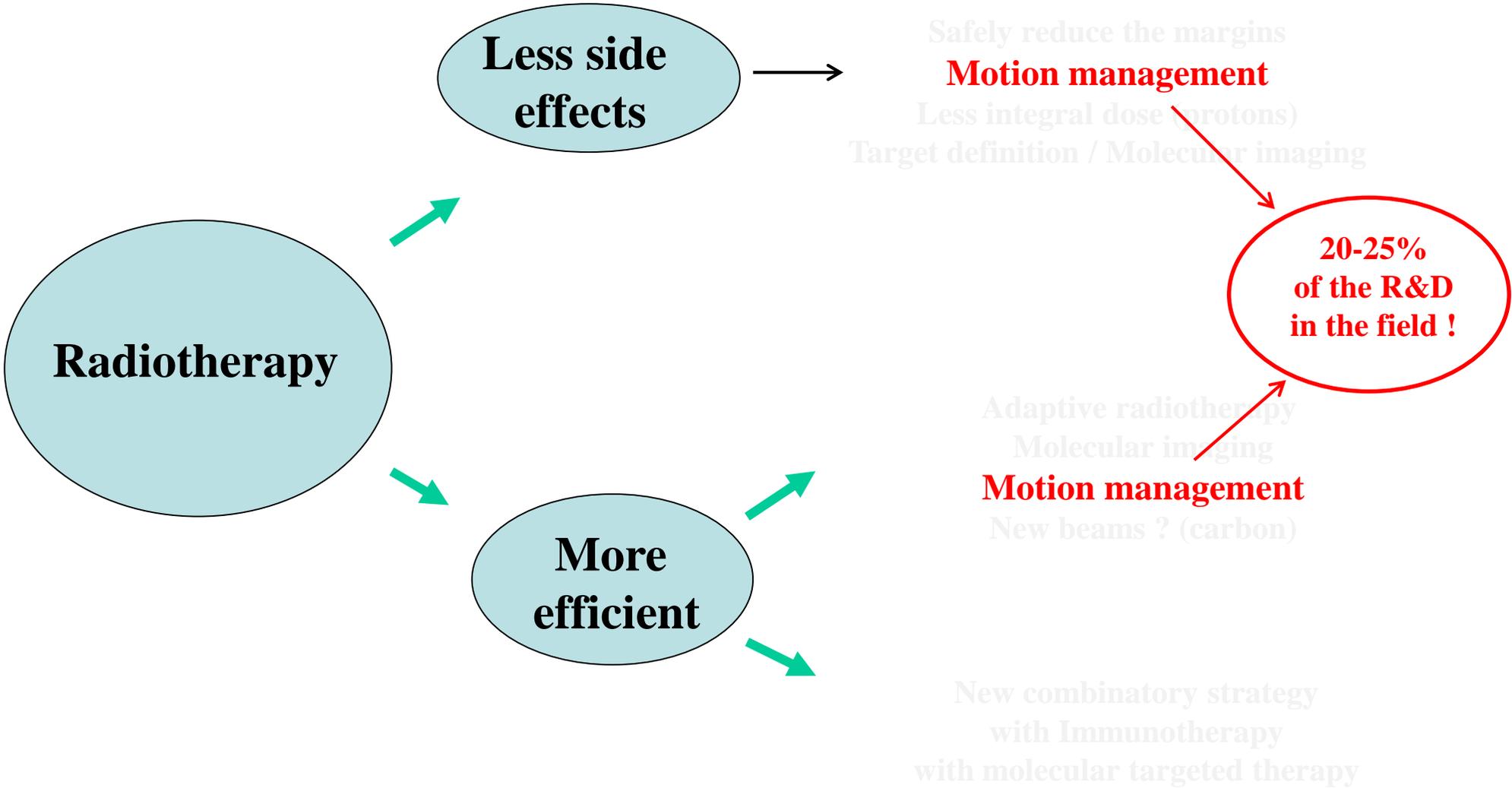
# Less and less normal tissues irradiated ...



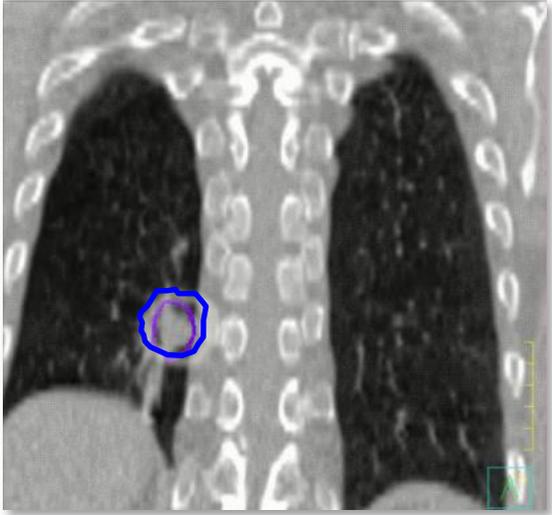
# Why is the volume effect so powerful in radiotherapy ?



# How to improve radiotherapy ?...



## How to mitigate motion management ?

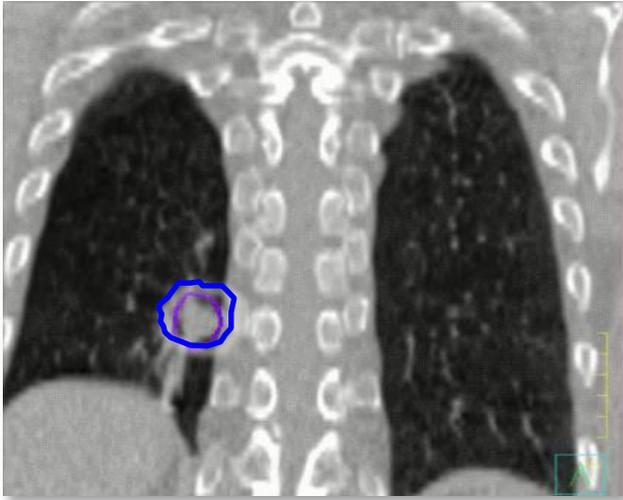


- **Respiratory gating / breath hold techniques**  
(ABC ...)
- **Tracking** : Calypso, CyberKnife,  
ViewRay, Linac-MRI ... etc ...



**New avenues ?**

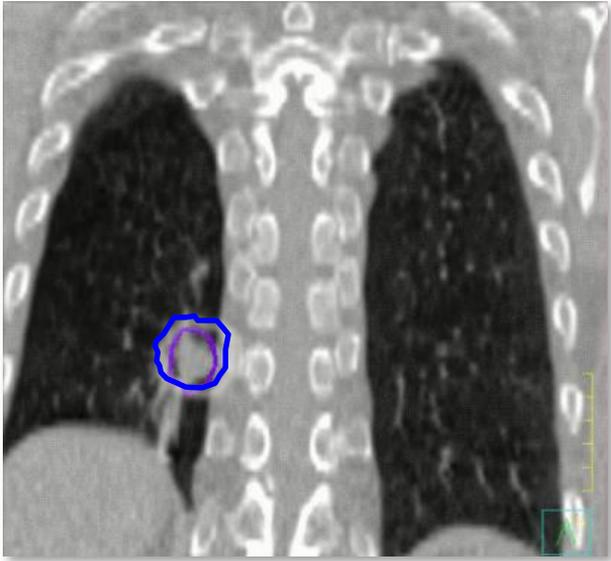
# How to mitigate motion management : new avenues ...?



- Respiratory gating, breath hold techniques (ABC ...)
- Tracking : Calypso, CyberKnife, ViewRay, Linac-MRI ... etc ...

- **Not breathing at all ... ?**
- **Extremely rapid RT system ?**

## How to mitigate motion management : new avenues ?



- Respiratory gating
- Breath hold techniques (ABC ...)
- Tracking calypso, CyberKnife, ViewRay, Linac-MRT ... etc ...

- **Not breathing at all ... ?**
- Extremely rapid RT system ?

# Not breathing at all ?

RADION 6640  
16 November 2015

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No. of Pages 7, Model 5G

Radiotherapy and Oncology xxx (2015) xxx–xxx

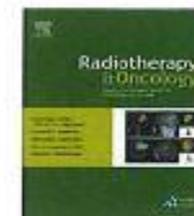


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Original article

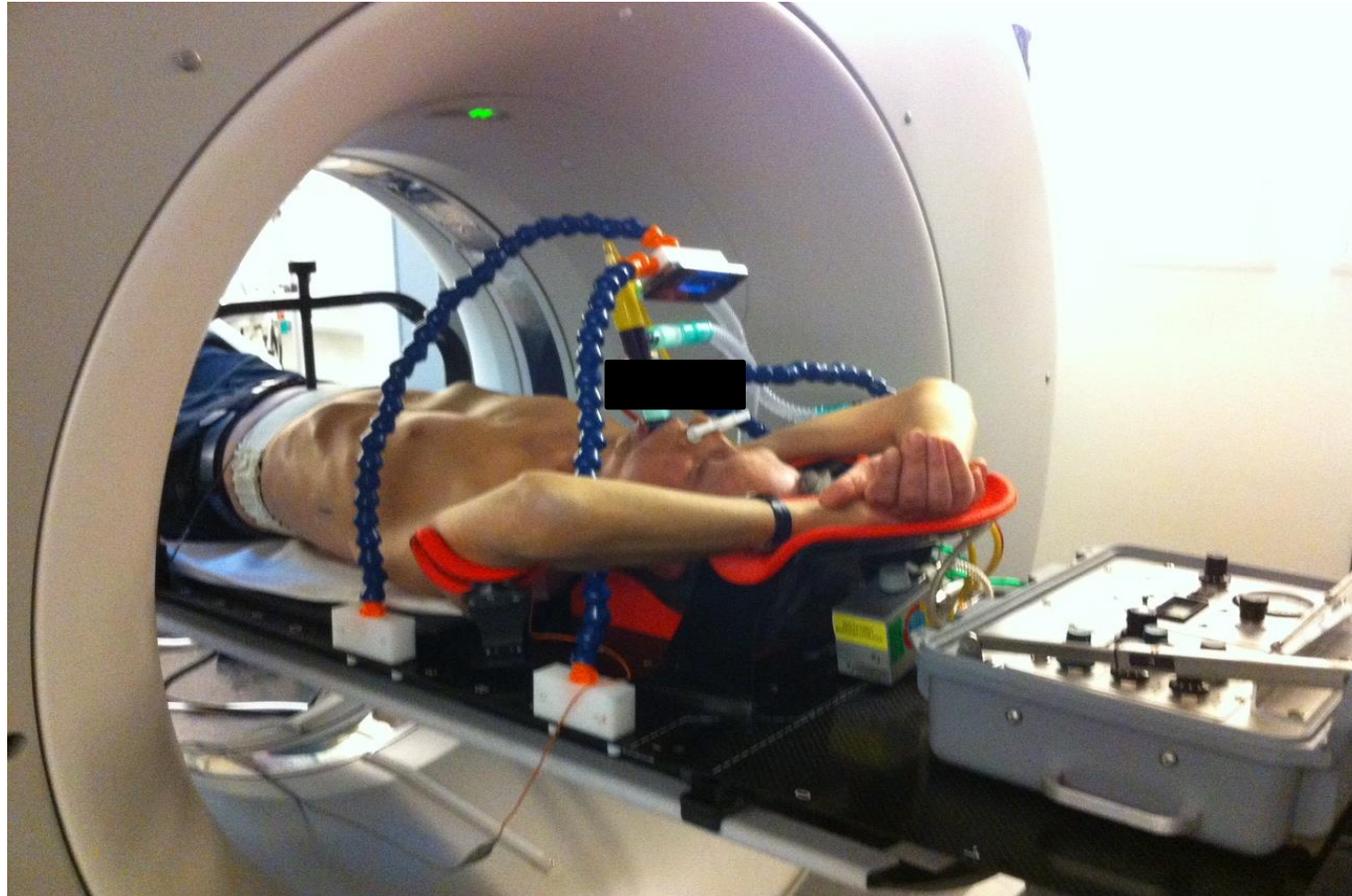
## Apnea-like suppression of respiratory motion: First evaluation in radiotherapy

Nicolas Péguret<sup>a,1</sup>, Mahmut Ozsahin<sup>a,1</sup>, Michele Zeverino<sup>c</sup>, Bastien Belmondo<sup>b</sup>, André-Dante Durham<sup>a</sup>, Alban Lovis<sup>d</sup>, Julien Simons<sup>b</sup>, Olivier Long<sup>b</sup>, Frédéric Duclos<sup>a</sup>, John Prior<sup>e</sup>, Alban Denys<sup>e</sup>, Catherine Beigelman<sup>e</sup>, Wendy Jeanneret Sozzi<sup>a</sup>, Kathleen Grant<sup>b</sup>, Véronique Gautier-Dechaud<sup>f</sup>, Solange Peters<sup>a</sup>, Monique Vienne<sup>f</sup>, Raphael Moeckli<sup>c</sup>, Jean Bourhis<sup>a,\*</sup>

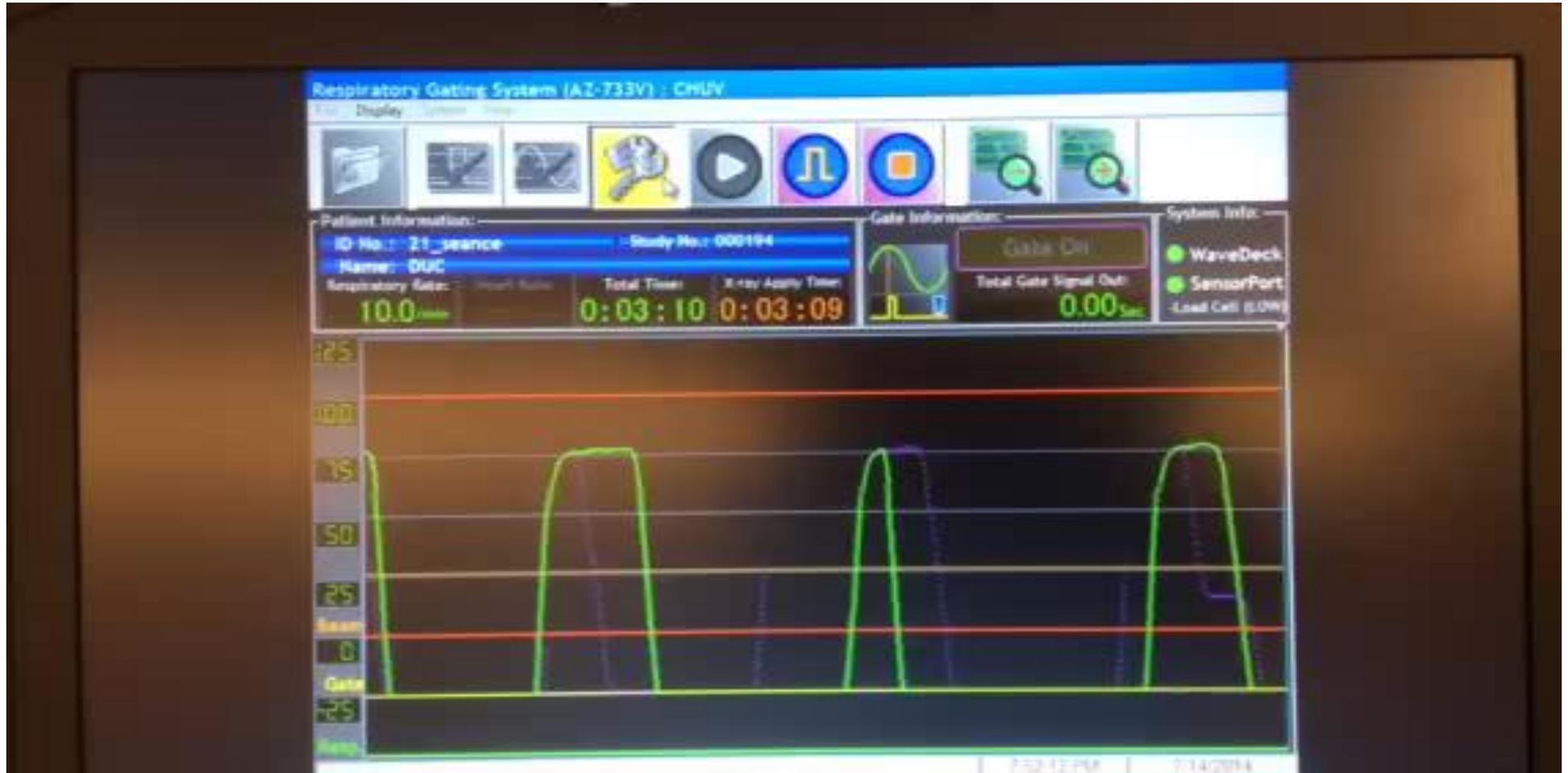
<sup>a</sup> Department of Oncology; <sup>b</sup> Department of Physiotherapy; <sup>c</sup> Institute of Radiation Physics; <sup>d</sup> Department of Pneumology; <sup>e</sup> Department of Radiology, Centre Hospitalier Universitaire Vaudois and University of Lausanne, Switzerland; <sup>f</sup> The BIRD Institute of Pulmonary Care, Villeneuve-Loubet, France

# Not breathing at all : PART

Percussion Assisted Radiotherapy  
(CHUV)



# PART : example for a patient with a breast cancer

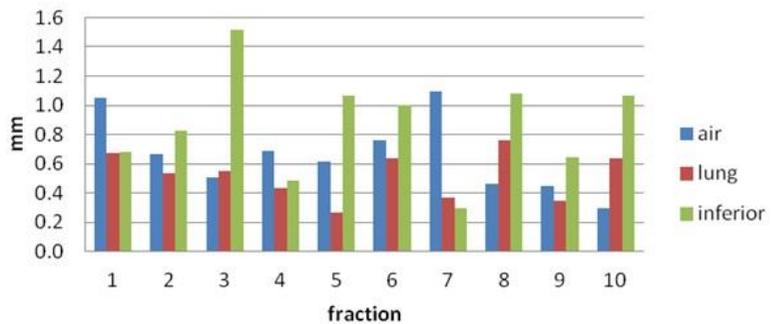


# **PART** : imaging the breast during treatment



# PART : First patient with breast cancer, 34 years old

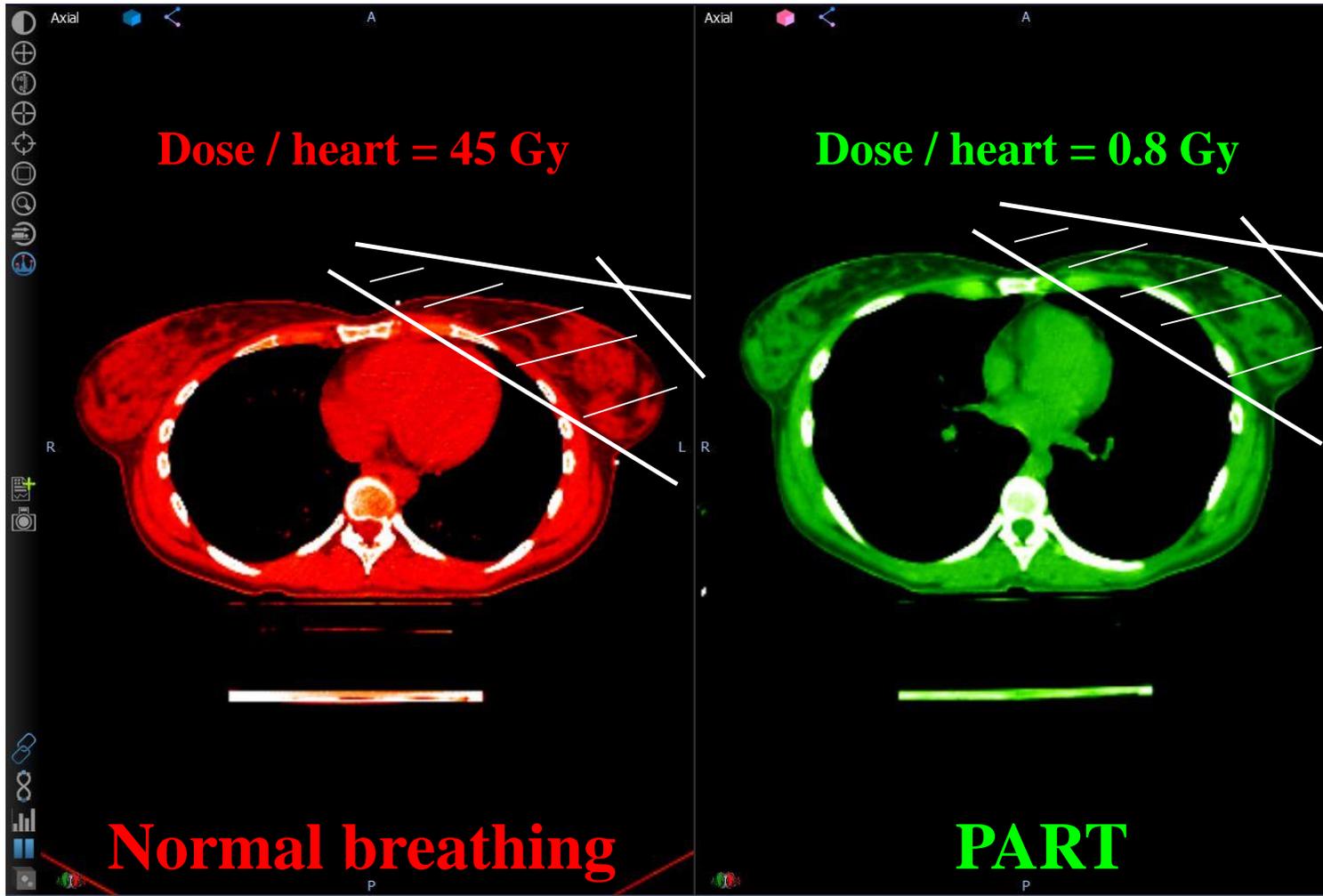
Breast motion  
 $\sigma$



Mean stabilisation time  
for “beam on”  
= 5 minutes 41 sec



# PART : any dosimetric gain ?...



# PART : any dosimetric gain ?...

	Free breathing	Maximal inspiration	PART
Mean heart dose	4.1 Gy	0.5 Gy	0.57 Gy
<b>Left Lung</b>			
V20	16%	10.5%	9.3%
V5	25%	20.6%	18%

*FB = Free Breathing, MI = Maximal Inspiration*

Fig b. Dosimetric parameters comparing FB /MI/PART for breast cancer

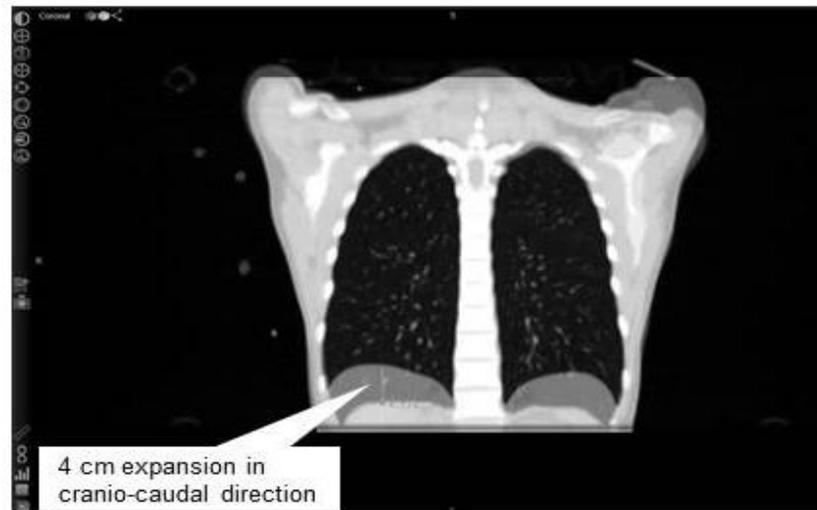
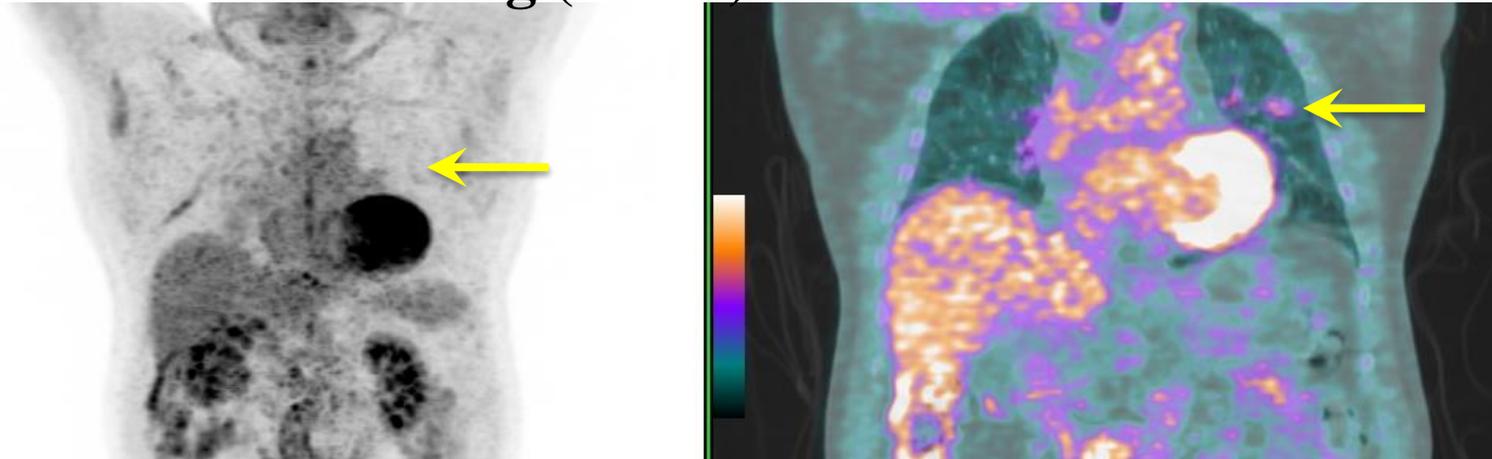


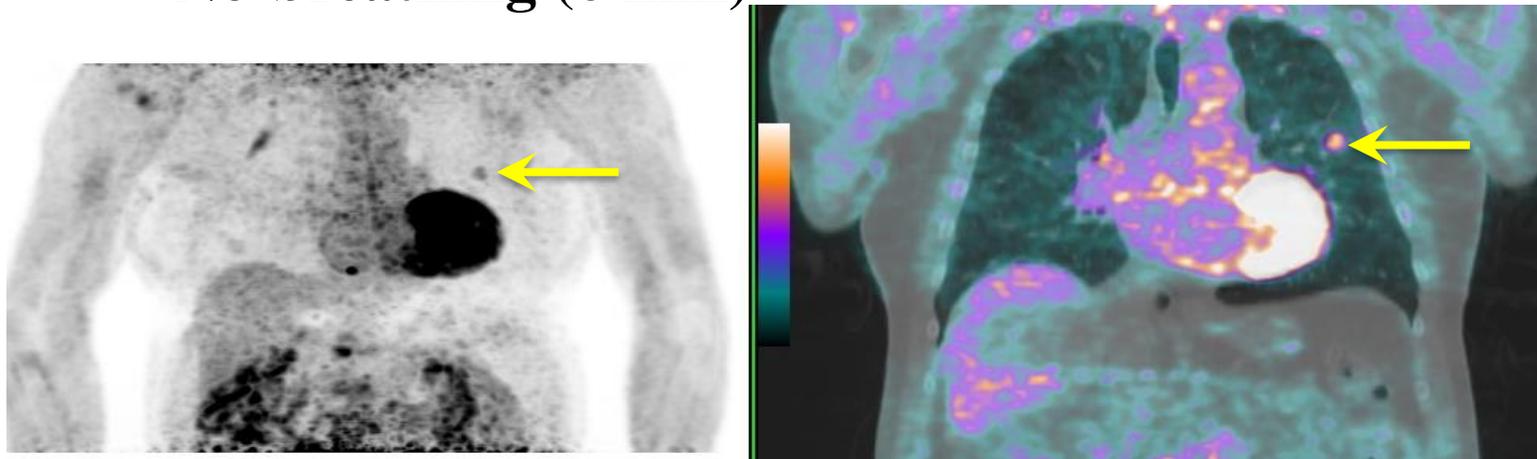
Fig d. Expansion of lungs in PART conditions compared to maximal inspiration

# Percussion Assisted PET-CT *(Prior et al JNM, 2016)*

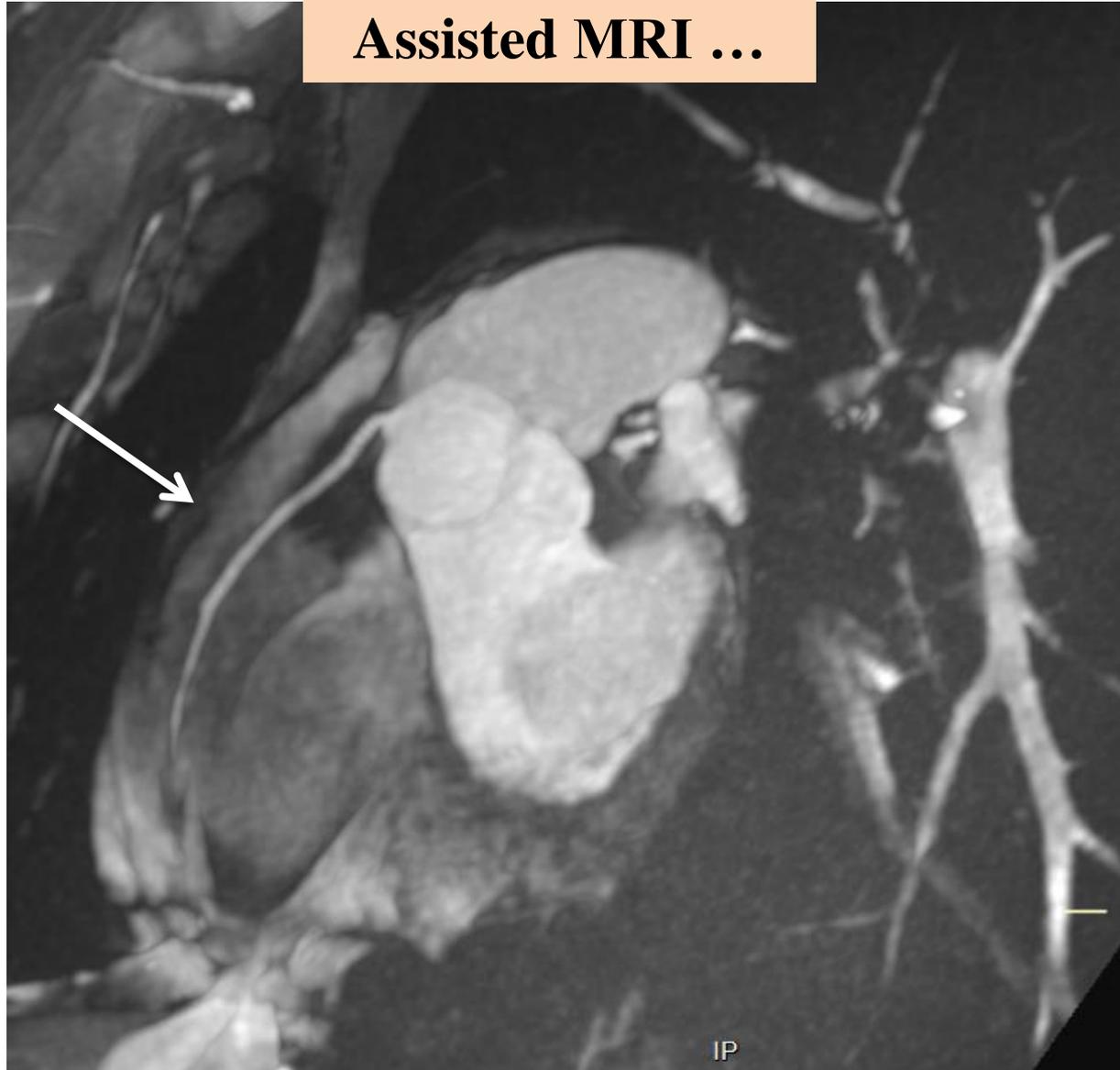
**Free-breathing (6 min)**



**No-breathing (6 min)**

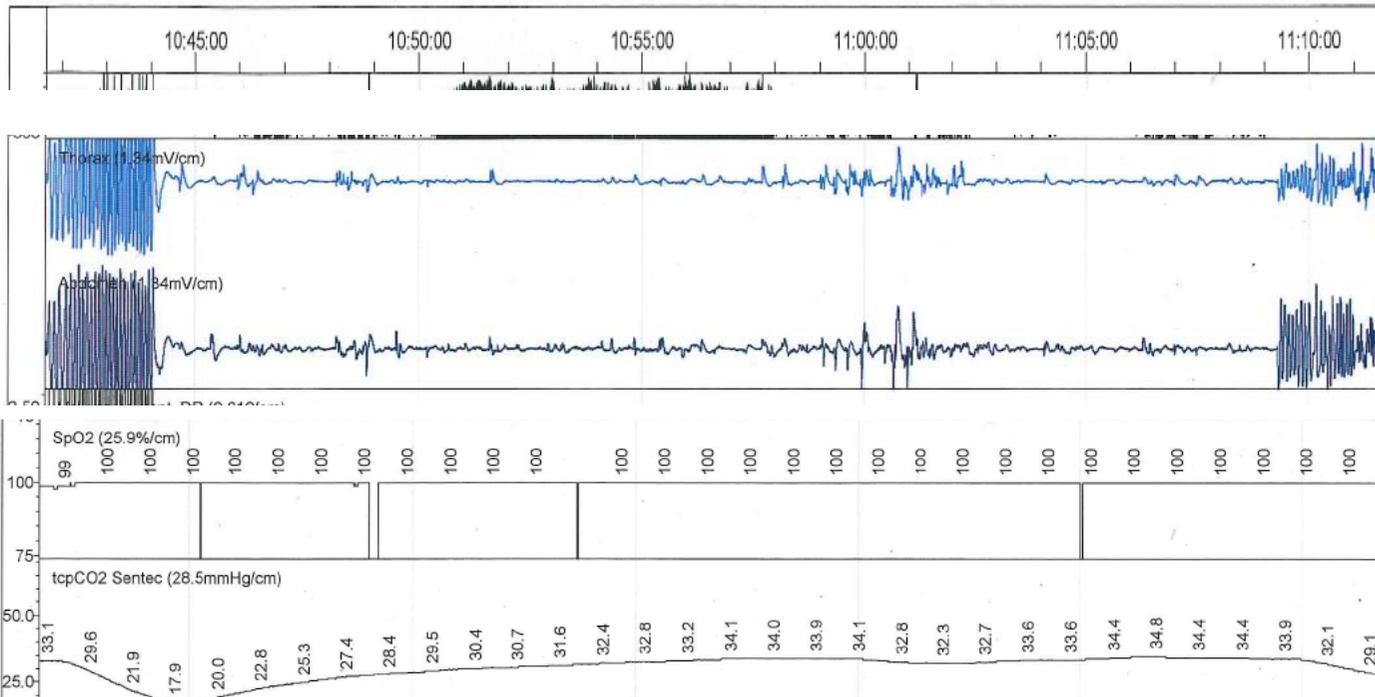


**Percussion  
Assisted MRI ...**



# From the first ... to ...the second generation of PART ...

25 minutes



# How useful is PART ?

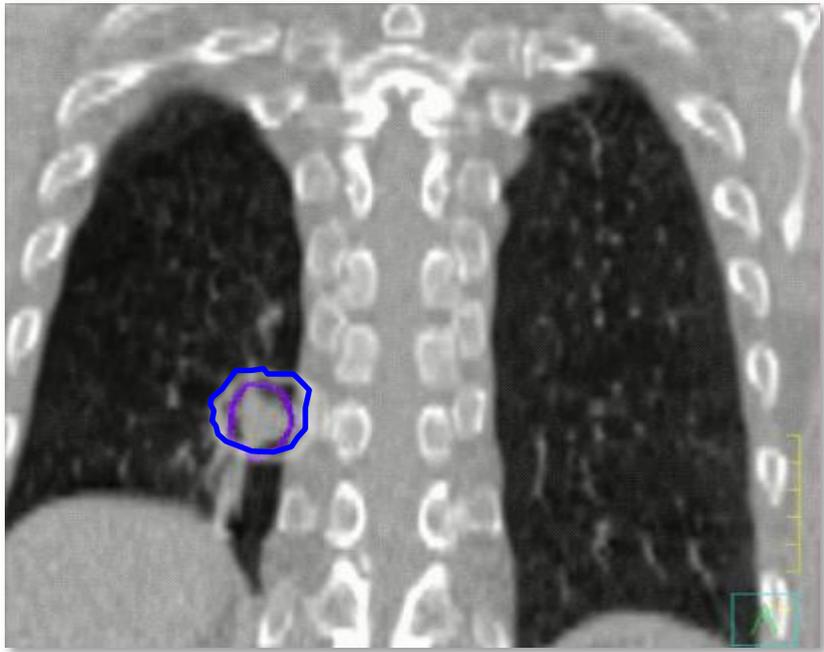
→ Ongoing clinical comparisons with gating / ABC and tracking systems



## The CHUV PART team !!

with Pneumologists (A Lovis) and Physiologists (K Grant)

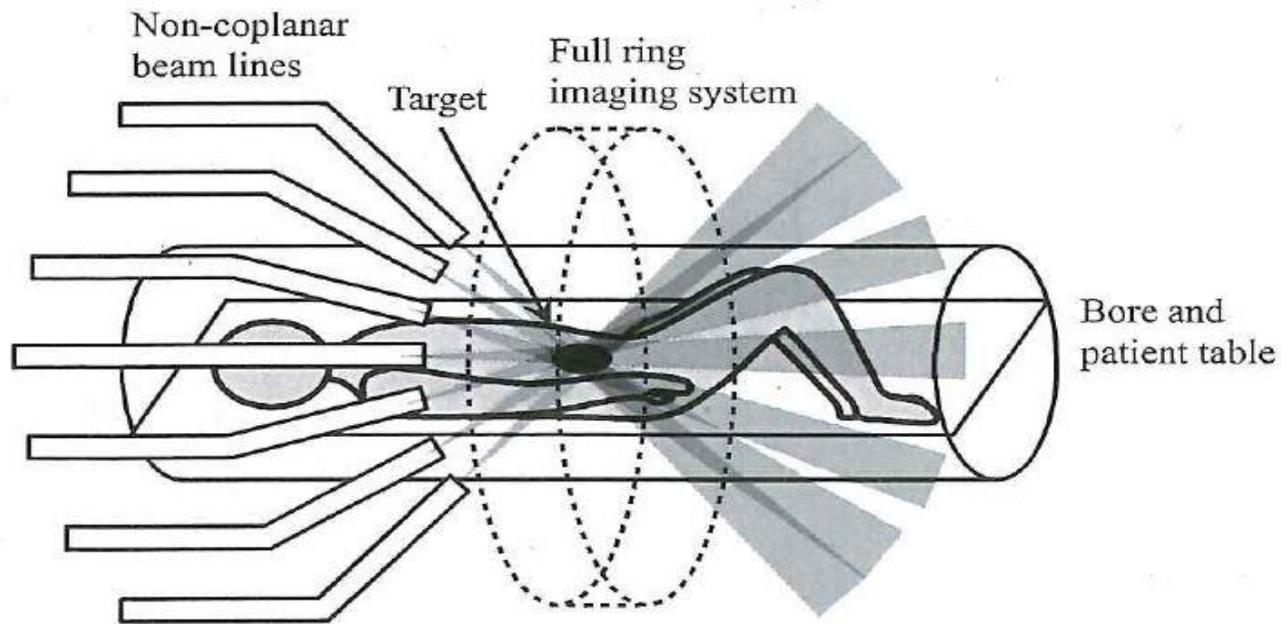
# How to mitigate motion management: new avenues ?



- Respiratory gating
- Breath hold techniques (ABC ...)
- Tracking calypso, CyberKnife, ViewRay, Linac-MR ... etc ...

- No breathing at all ... ?

**- Extremely rapid RT system ?**



Extremely rapid radiation therapy setup.

*Stanford University*

**PLURIDIRECTIONAL VERY HIGH  
ELECTRON ENERGY RADIATION THERAPY  
SYSTEMS AND PROCESSES**

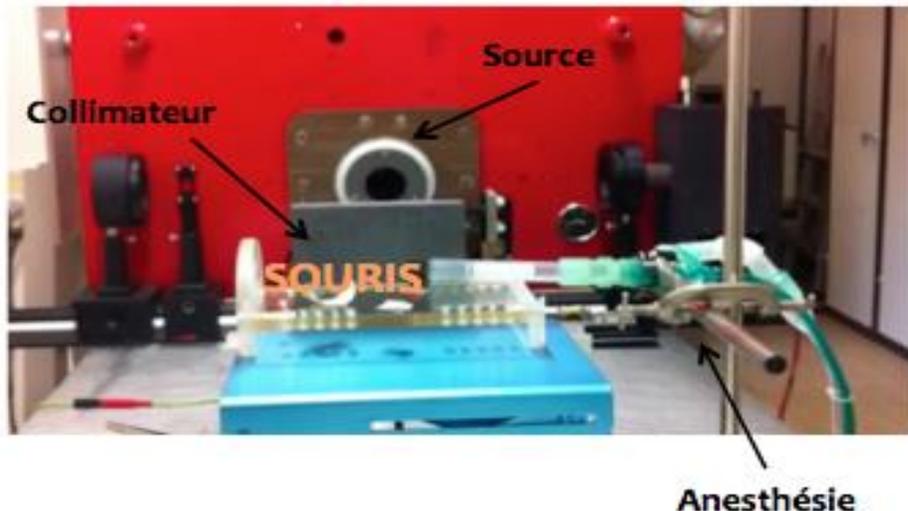
**CROSS-REFERENCES TO RELATED  
APPLICATIONS**

**[0001]** The present application claims the benefit under 35 USC 119(e) of US Provisional Application No. 61/606,408 filed Mar. 3, 2012; the full disclosure of which is incorporated herein by reference in its entirety.

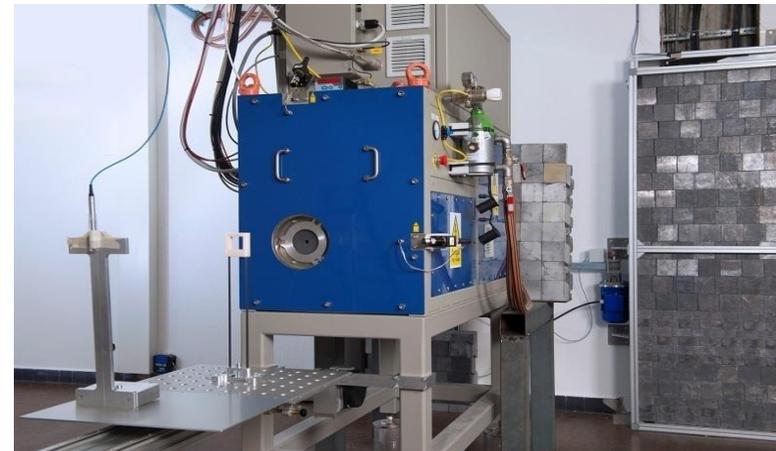
## Other example of extremely rapid radiation therapy set-up : FLASH

	CDR	Flash
Dose rate	0,04 Gy / sec	<b>50 Gy / sec</b>
Time for 20 Gy	500 sec ( $\approx$ 8 min)	<b>400 ms</b>

...with CURIE LINAC 4,5 MeV



...with CHUV LINAC 6 MeV



## 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>



V Favaudon



MC Vozenin

www.ScienceTranslationalMedicine.org 16 July 2014 Vol 6 Iss

## RESEARCH HIGHLIGHTS

## IN BRIEF


**RADIOTHERAPY**  
 FLASHing tumours

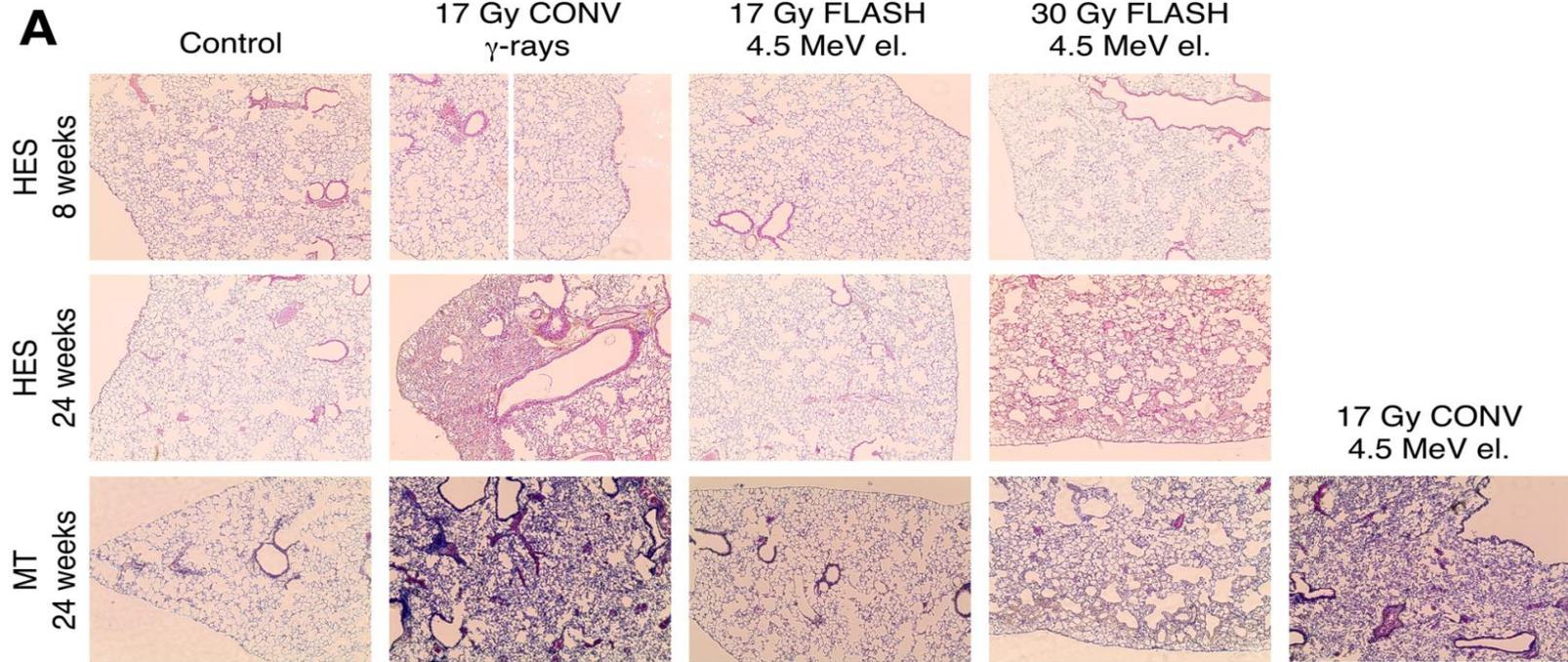
A new study in mice suggests that radiation delivered in short pulses at ultrahigh dose rates (FLASH) is as effective against lung tumours as conventional protracted single lower dose rates and has fewer side effects. Using both orthotopic lung tumours in immunocompetent mice and human lung tumour xenografts in nude mice, Favaudon *et al.* showed that FLASH irradiation caused less lung fibrogenesis and less apoptosis in normal tissue than conventional radiation. Although this technique was only tested in one tumour type, it suggests that delivery methods are crucial to minimizing radiation treatment side effects, and it has implications for therapeutic protocols.

**ORIGINAL RESEARCH PAPER** Favaudon, V. *et al.* Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice. *Sci. Transl. Med.* **6**, 245ra93 (2014)

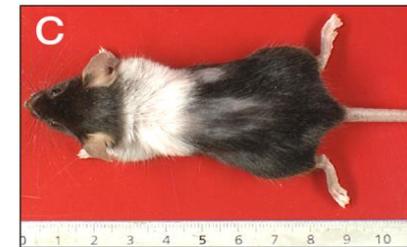


# Flash-RT induces less lung fibrosis ...

n=300 C57BL /6J



1



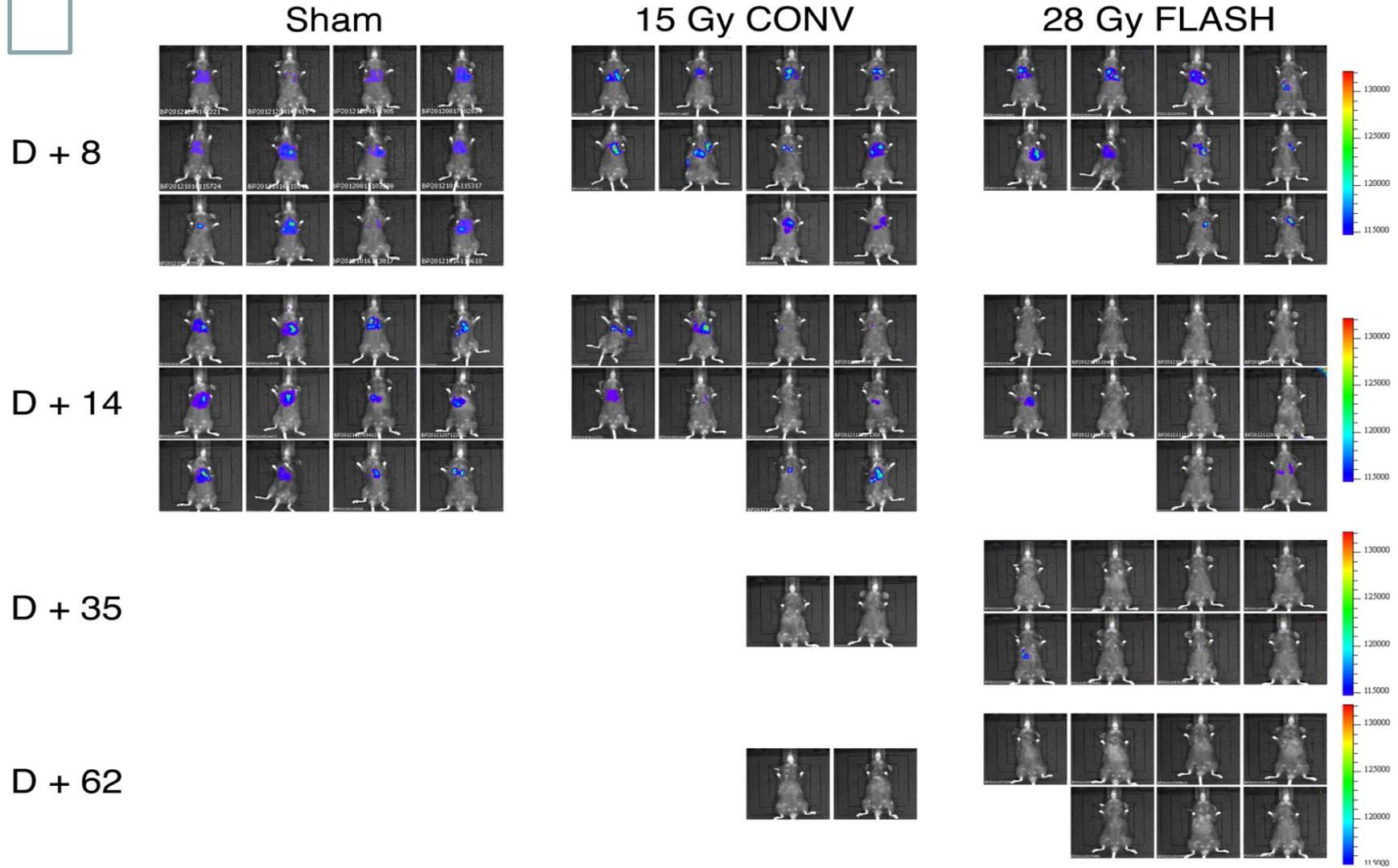


# Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice

Vincent Favaudon *et al.*

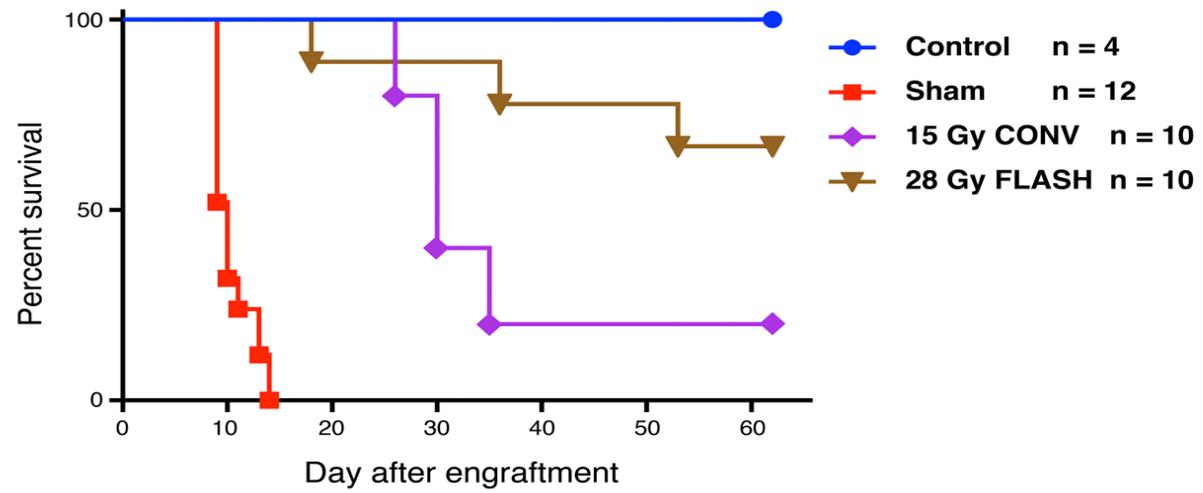
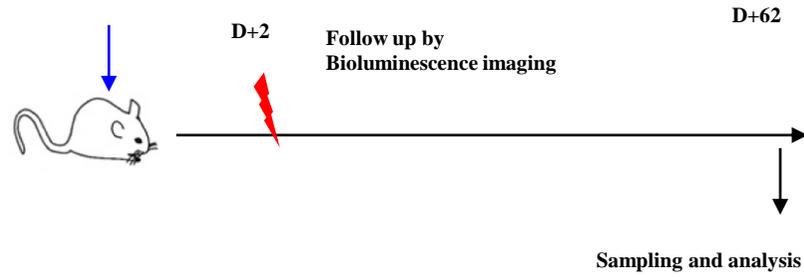
*Sci Transl Med* **6**, 245ra93 (2014);

DOI: 10.1126/scitranslmed.3008973





**D0 orthotopic implantation of 500 000 Luc+ TC-1 in the lung**



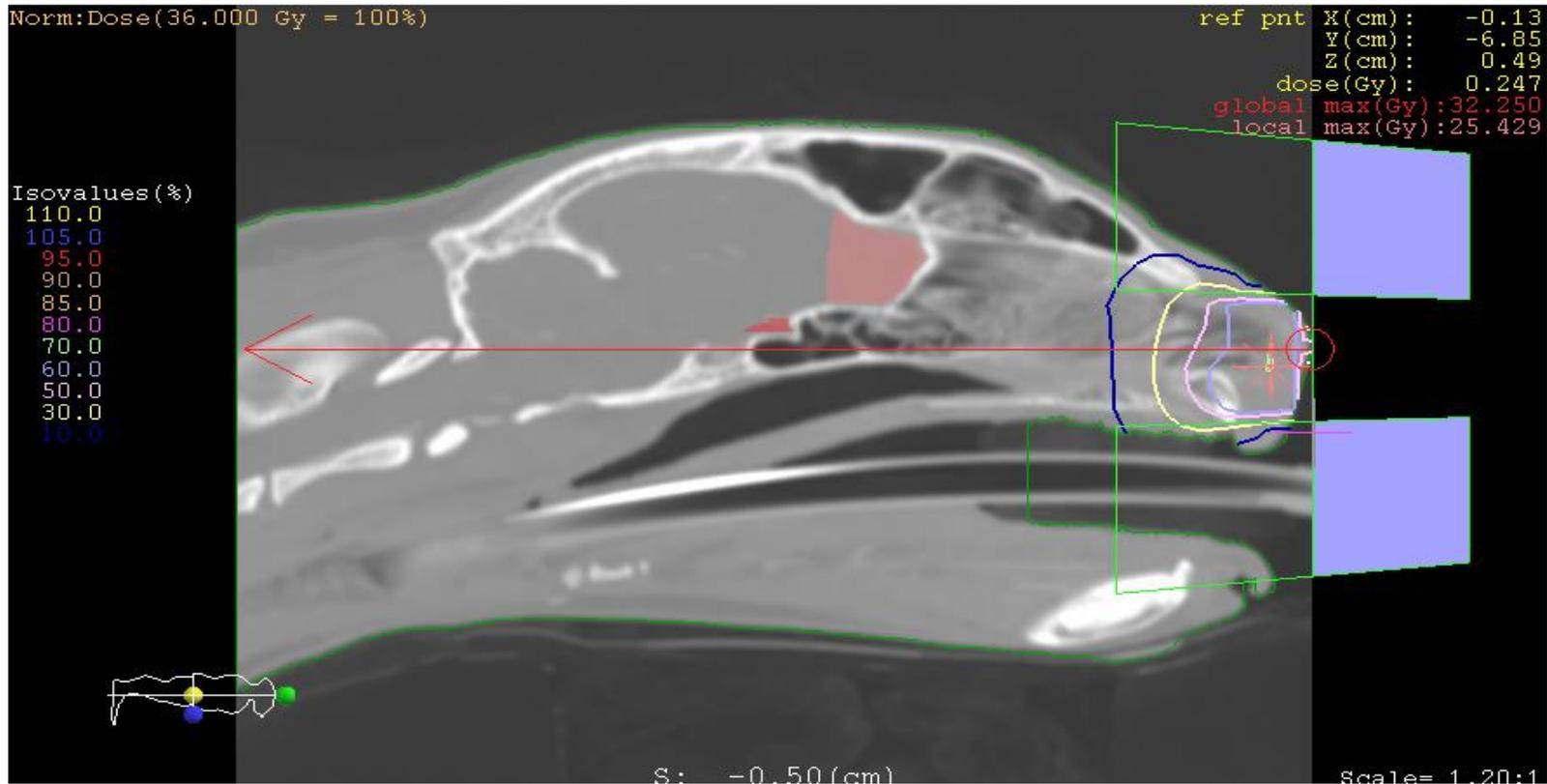
# FLASH-RT in cat with spontaneous cancer ?



**29<sup>th</sup> of sept 2015**

***11 year old male, 7 kg with a nasal squamous cell carcinoma***

# FLASH-RT in cat



Reconstructed dose distribution according to a measured **single dose of 31 Gy** at the skin surface.

**26th November 2015, 2 months**



# Potential interest of extremely rapid radiotherapy set-up?

- Ultra fast : no intra-fraction **motion** management
- No irradiation of circulating lymphocytes (better **immune** response ?)
- Perhaps a more pronounced **differential effect** ? (*ex : Flash : tumor vs normal tissues ; Favaudon 2014 ...*)
- Is the effect on hypoxic cells the same ? (*all electron deposit at the same time, is it mimicking a higher LET effect ?*)
- Potential for markedly **reducing** the radiotherapy workload ?



## Radiobiology team

MC Vozenin  
B Petit  
J Ollivier  
P Montay-Gruel  
G Boivin  
P Tsoutsou  
F Herrera  
A Durham

## IRA team

F Bochud  
JF Germond  
C Bailat  
M Jaccard  
K Petersson  
J Damet  
N Cherbuin

## Radio-Onco team

J Bourhis  
M Oszahn  
H Bouchaab

## Curie team

V Favaudon  
J Hall  
C Feuillade  
F Pouzoulet

## CEA team

PH Romeo  
F Pflumio  
N Gault  
D Lewandowski  
F Hoffchir  
S Moreno  
B Uzan

## EPFL team

D Hanahan team  
E Meylan team