Novel Innovations in Proton Therapy

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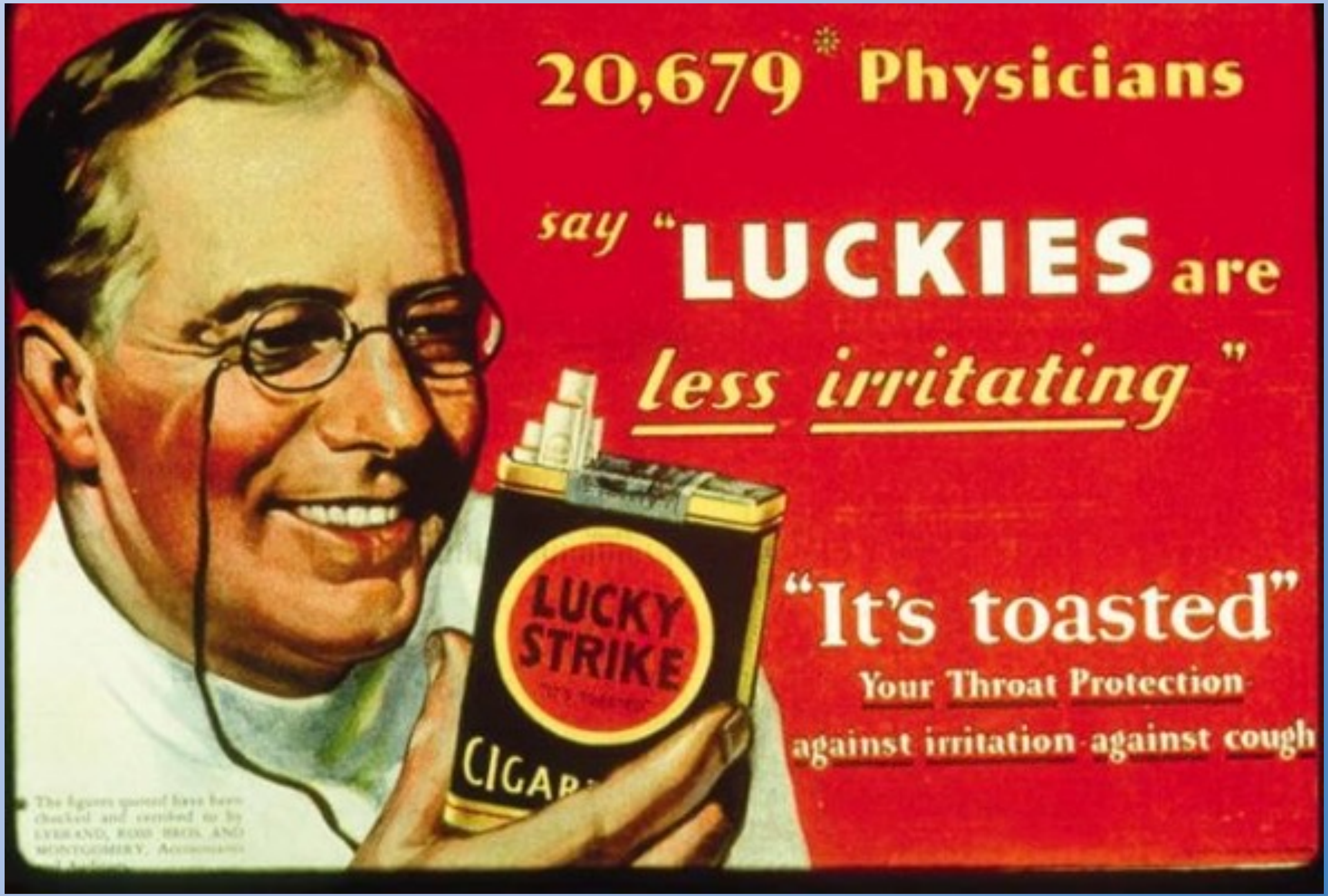
Medical Director

South Florida Proton Therapy Institute



Conflicts: None


The Economist
The state of the race
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SURVEY OF IRELAND
Beating cancer
The new frontier of molecular medicine


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THERE IS NEW AMMUNITION IN THE WAR AGAINST
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THESE ARE THE BULLETS.
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BusinessWeek
DRUGS GET SMART
How new medicines will more effectively target what ails you —and help prevent another Vioxx


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NEW DIGITAL TELEVISIONS
Forbes
She was 18 and dying of lung cancer. This pill saved her life—but failed to help almost everyone else. Should it be approved?
MIRACLE PILL
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THE RICHEST PEOPLE IN CHINA
DIVIDEND HEIST: WHEN COMPANIES WANT THEM BACK


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MUTUAL FUNDS FOR THE LONG HAUL
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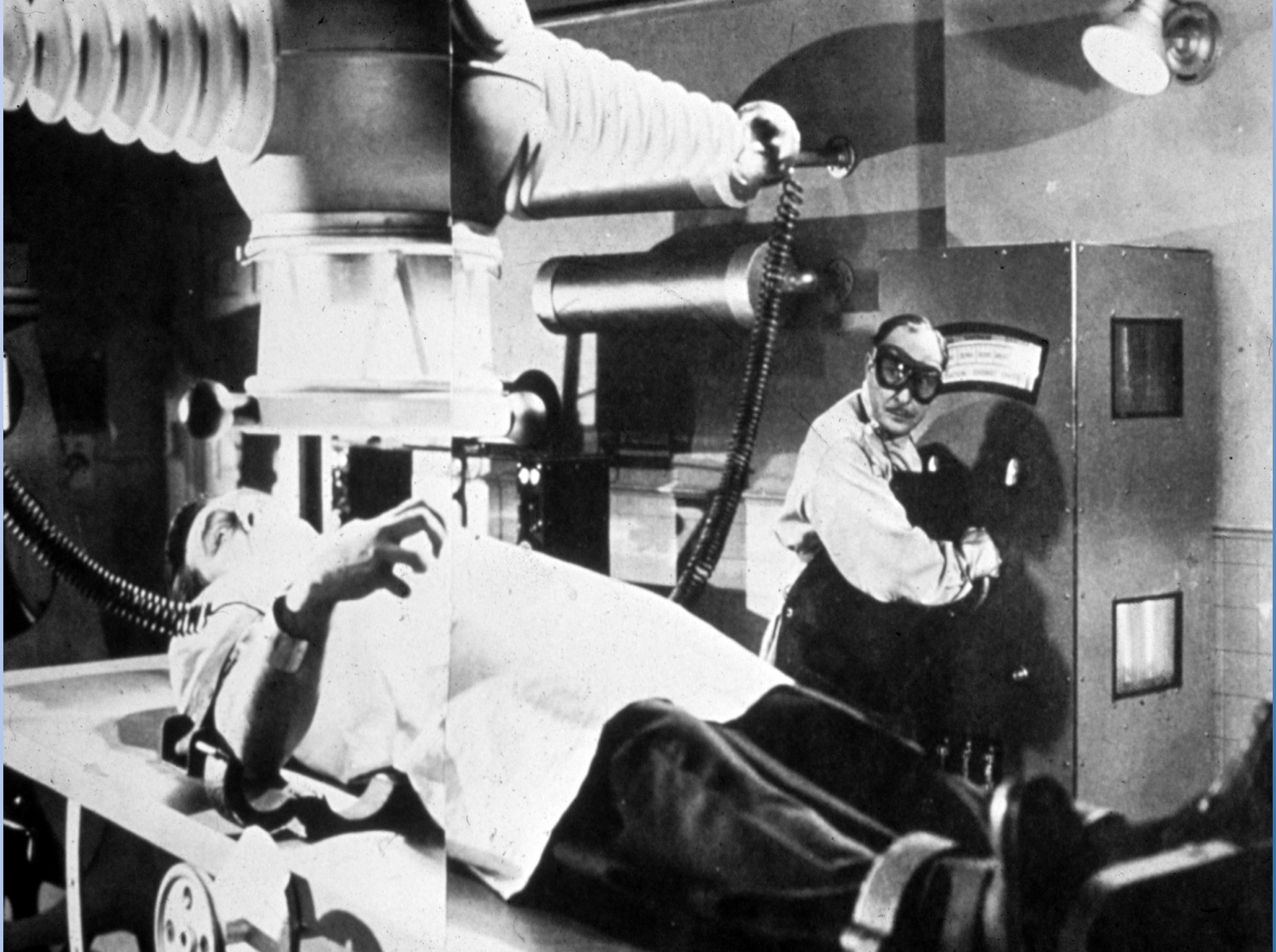
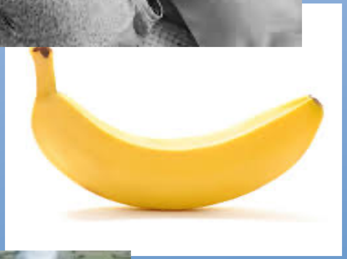
THIS DRUG'S FOR YOU
NEW TARGETED MEDICINES PROMISE BREAKTHROUGH CURES

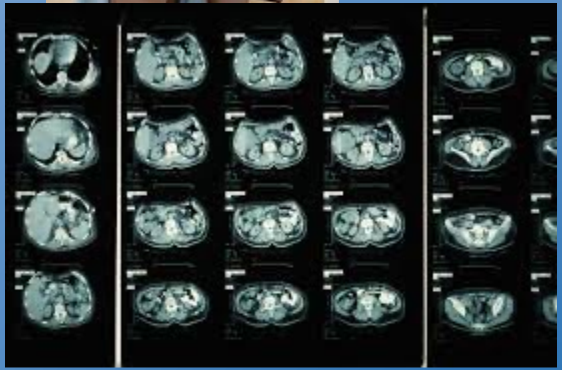


Activity	Dose (rads)
Average background radiation dose, typical day	**0.001**
Sleeping next to someone, 8 hours	0.000005
Eating one banana	0.00001
Living within 50 miles of a nuclear power plant for a year	0.00001
Living within 50 miles of a coal-fired power plant for a year	0.00003
Dental x-ray	0.0005
Airline flight from New York to Los Angeles	0.004

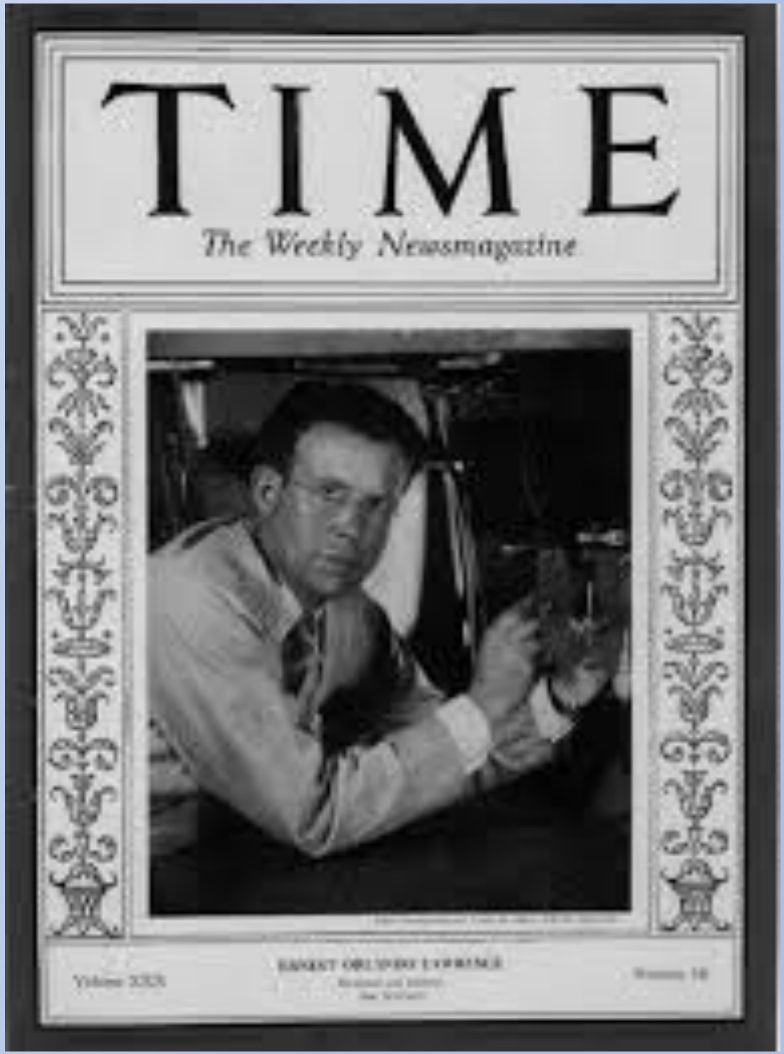



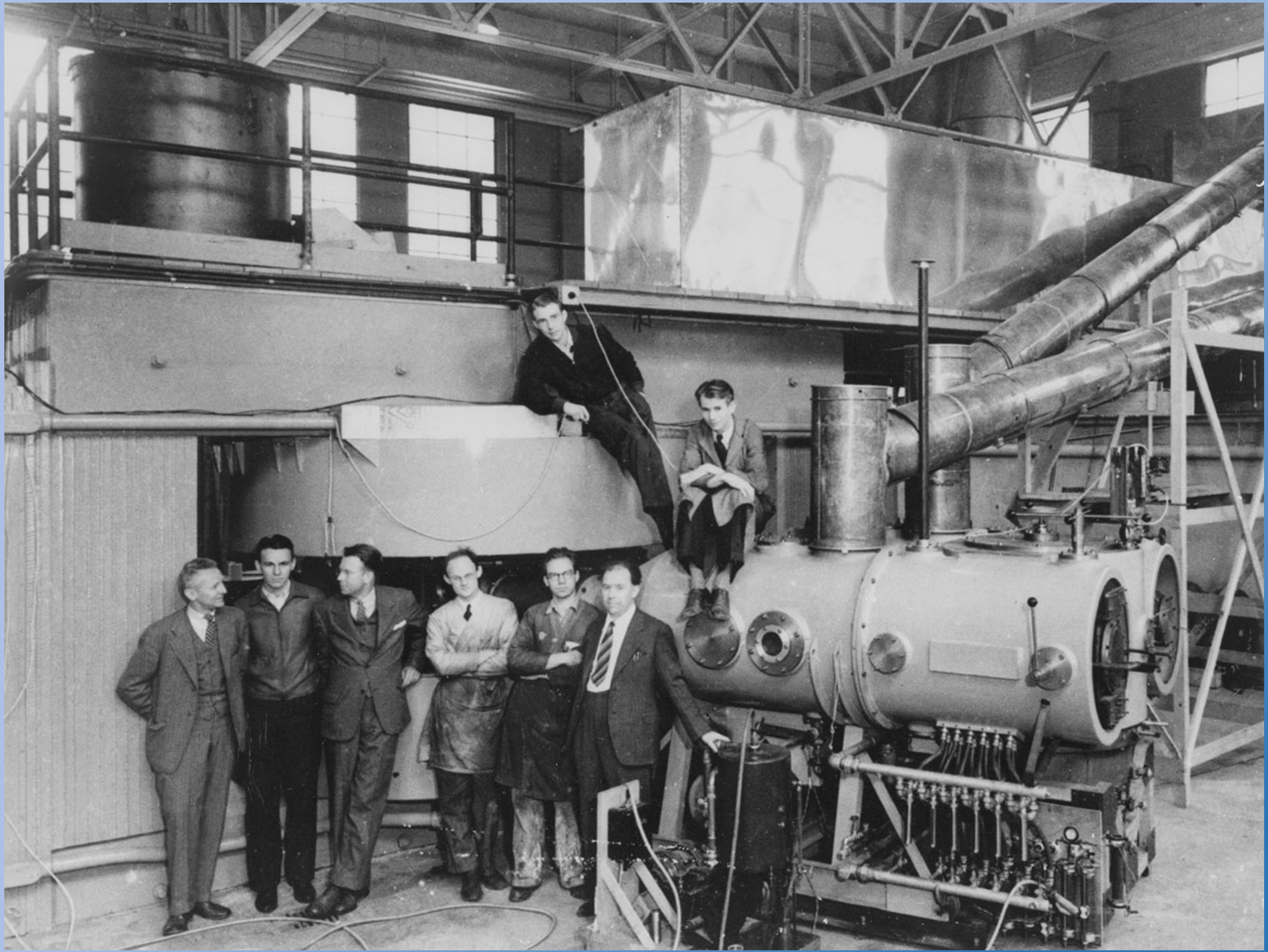

Activity	Dose (rads)
Average background radiation dose, typical day	**0.001**
Living in a concrete building for a year	0.007
Yearly dose from naturally occurring P-32 in your body	0.039
Screening mammogram	0.04
CT Brain	0.2
CT Chest	0.7
Dose from one hour exposure on the grounds at Chernobyl in 2010	0.6






Activity	Dose (rads)
Average background radiation dose, typical day	**0.001**
Maximum yearly dose allowed for US radiation workers	5.0
Lowest annual dose clearly related to increased cancer risk	100
Typical localized daily dose in radiation oncology	200
Whole-body dose causing non-fatal radiation poisoning	200
Whole body single fraction fatal dose	400
Ten minutes next to reactor core, Chernobyl after explosion and meltdown	5000


TIME
The Weekly Newsmagazine

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SPECIALIZED INC.
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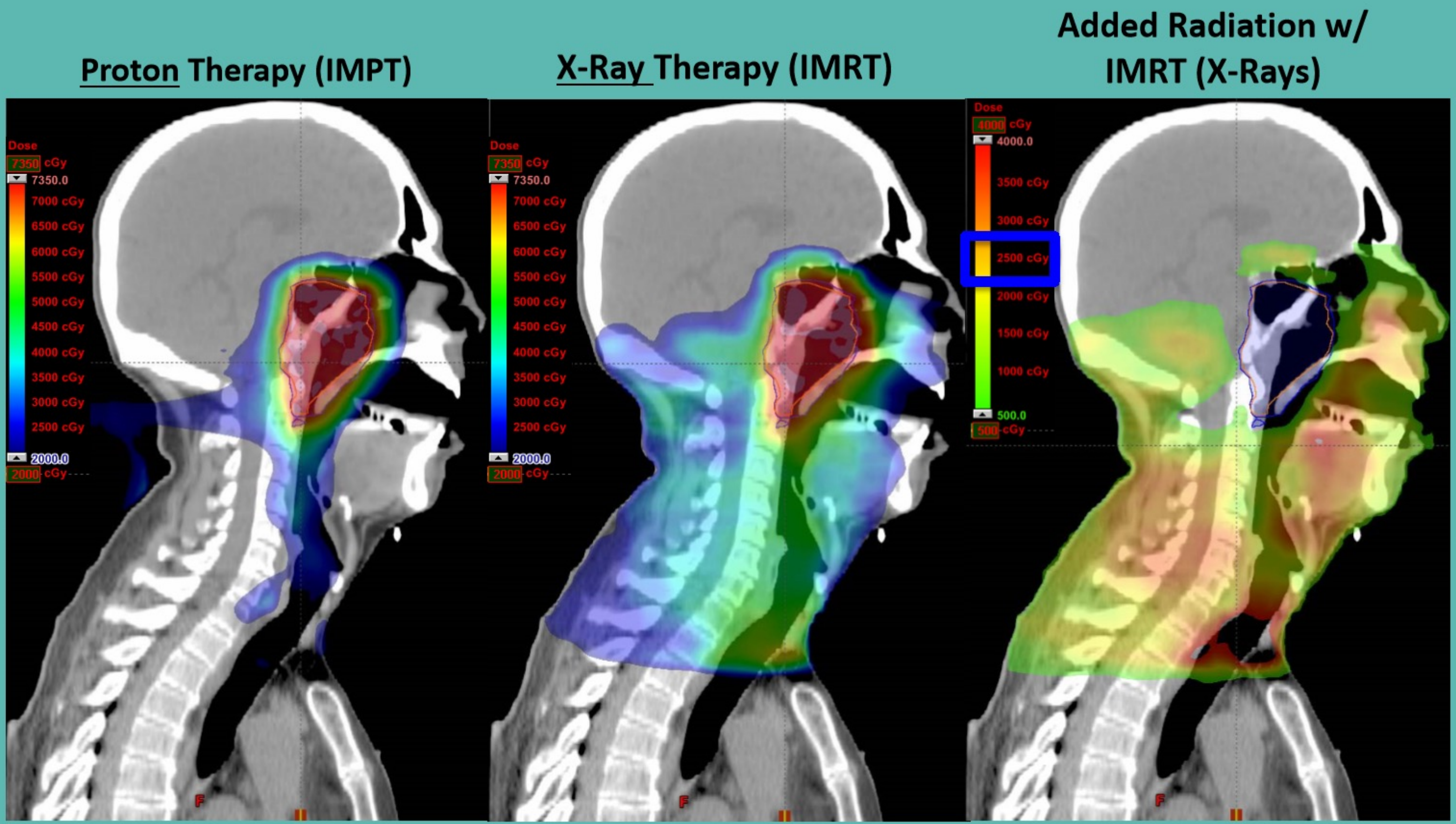
BEYEL

ELIMINATION OF UNNECESSARY RADIATION



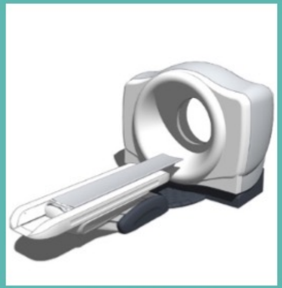
***25 Gy (25 Sv) of Unnecessary Radiation**

Goughenour 2017

ELIMINATION OF UNNECESSARY RADIATION

Added Radiation w/
IMRT (X-Rays)

*25 Gy (25 Sv) of Unnecessary Radiation =

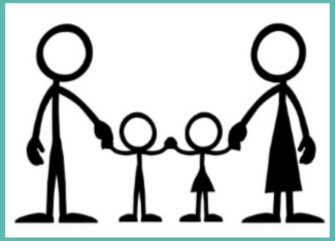


12,500

H&N CTs
(2 mSv)

5,000,000

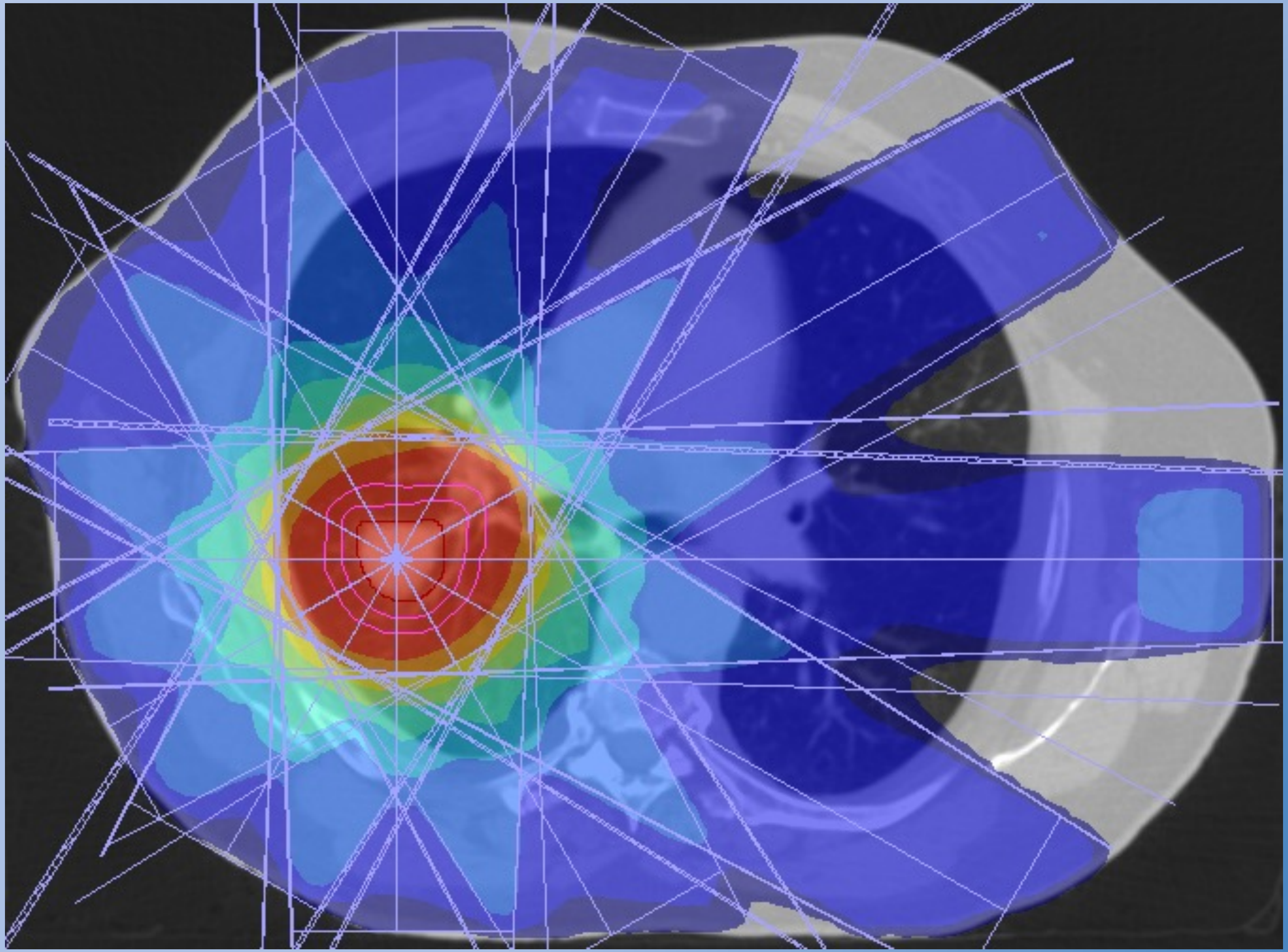
Intraoral X-Rays
(0.002 mSv)

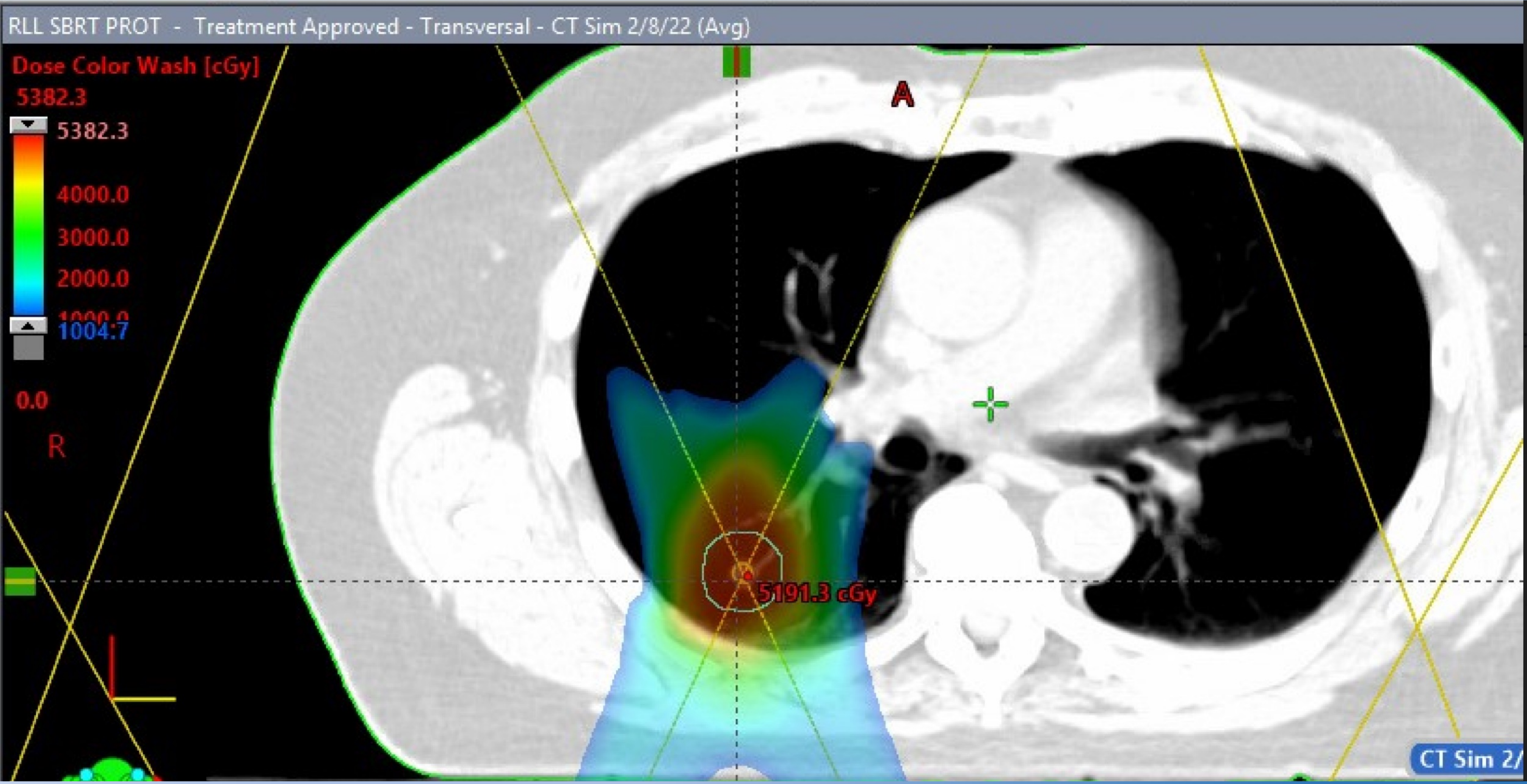


25,000x

General Public
Annual Limit (1.0 mSv)

Solitary Lung Nodule: Linac Based SBRT




RLL SBRT PROT - Treatment Approved - Transversal - CT Sim 2/8/22 (Avg)
Dose Color Wash [cGy]
5382.3
5382.3
4000.0
3000.0
2000.0
1004.7
0.0
R
A
5191.3 cGy
CT Sim 2/

Early Findings on Toxicity of Proton Beam Therapy With Concurrent Chemotherapy for Nonsmall Cell Lung Cancer

Samir Sejpal, MD[1]; Ritsuko Komaki, MD[1]; Anne Tsao, MD[2]; Joe Y. Chang, MD, PhD[1]; Zhongxing Liao, MD[1]; Xiong Wei, MD[1]; Pamela K. Allen, PhD[1]; Charles Lu, MD[2]; Michael Gillin, PhD[3]; and James D Cox, MD[1]

Table 2. Acute Nonhematologic Toxicity After Photon Versus Proton Therapy for Nonsmall Cell Lung Cancer

Toxicity and Treatment	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Unknown	*P*
Esophagitis								<.001
Chemotherapy+3D-CRT	3 (4)	25 (34)	33 (45)	13 (18)	0	0	0	
Chemotherapy+IMRT	4 (6)	9 (14)	24 (36)	26 (39)	3 (4.5)	0	0	
Chemotherapy+PBT	13 (21)	22 (35.5)	24 (39)	3 (5)	0	0	0	
Pneumonitis								<.001
Chemotherapy+3D-CRT	23 (31)	9 (12)	20 (27)	22 (30)	0	0	0	
Chemotherapy+IMRT	19 (29)	24 (36)	17 (26)	4 (6)	0	2 (3)	0	
Chemotherapy+PBT	13 (21)	30 (48)	18 (29)	1 (2)	0	0	0	
Dermatitis								<.001
Chemotherapy+3D-CRT	6 (8)	54 (73)	9 (12)	5 (7)	0	0	0	
Chemotherapy+IMRT	5 (8)	33 (50)	17 (26)	11 (17)	0	0	0	
Chemotherapy+PBT	2 (3)	22 (35.5)	23 (37)	15 (24)	0	0	0	
Fatigue								.002
Chemotherapy+3D-CRT	0	20 (24)	28 (34)	24 (29)	2 (2)	0	0	
Chemotherapy+IMRT	12 (18)	16 (24)	27 (41)	10 (15)	1 (1.5)	0	0	
Chemotherapy+PBT	3 (5)	12 (19)	32 (52)	12 (19)	3 (5)	0	0	

All data are expressed as No. of patients (%).

3D-CRT indicates 3-dimensional conformal radiation therapy; IMRT, intensity-modulated radiation therapy; PBT, proton beam therapy.

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Physica Medica

Volume 52, Supplement 1, August 2018, Page 22

[OA052] Proton minibeam radiation therapy: A promising alternative for high-grade gliomas

Yolanda Prezado [a], Wilfredo Gonzalez [a], Annalisa Patriarca [b], Gregory Jouvion [c], Consuelo Guardiola [a], Catherine Nauraye [b], Dalila Labiod [d], Marjorie Juchaux [a], Laurene Jourdain [e], Catherine Sebrié [e], Frederic Pouzoulet [d]

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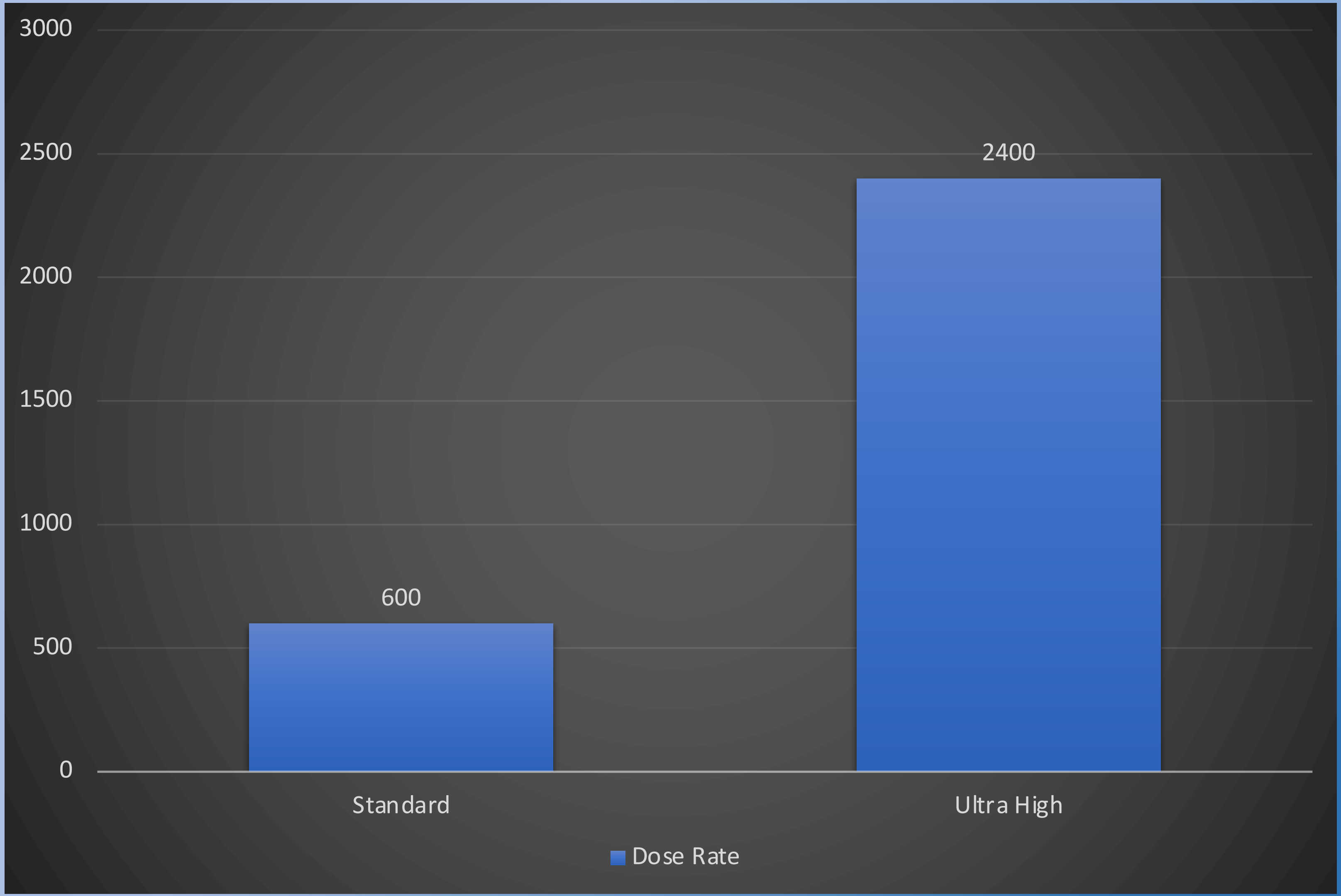
https://doi.org/10.1016/j.ejmp.2018.06.124



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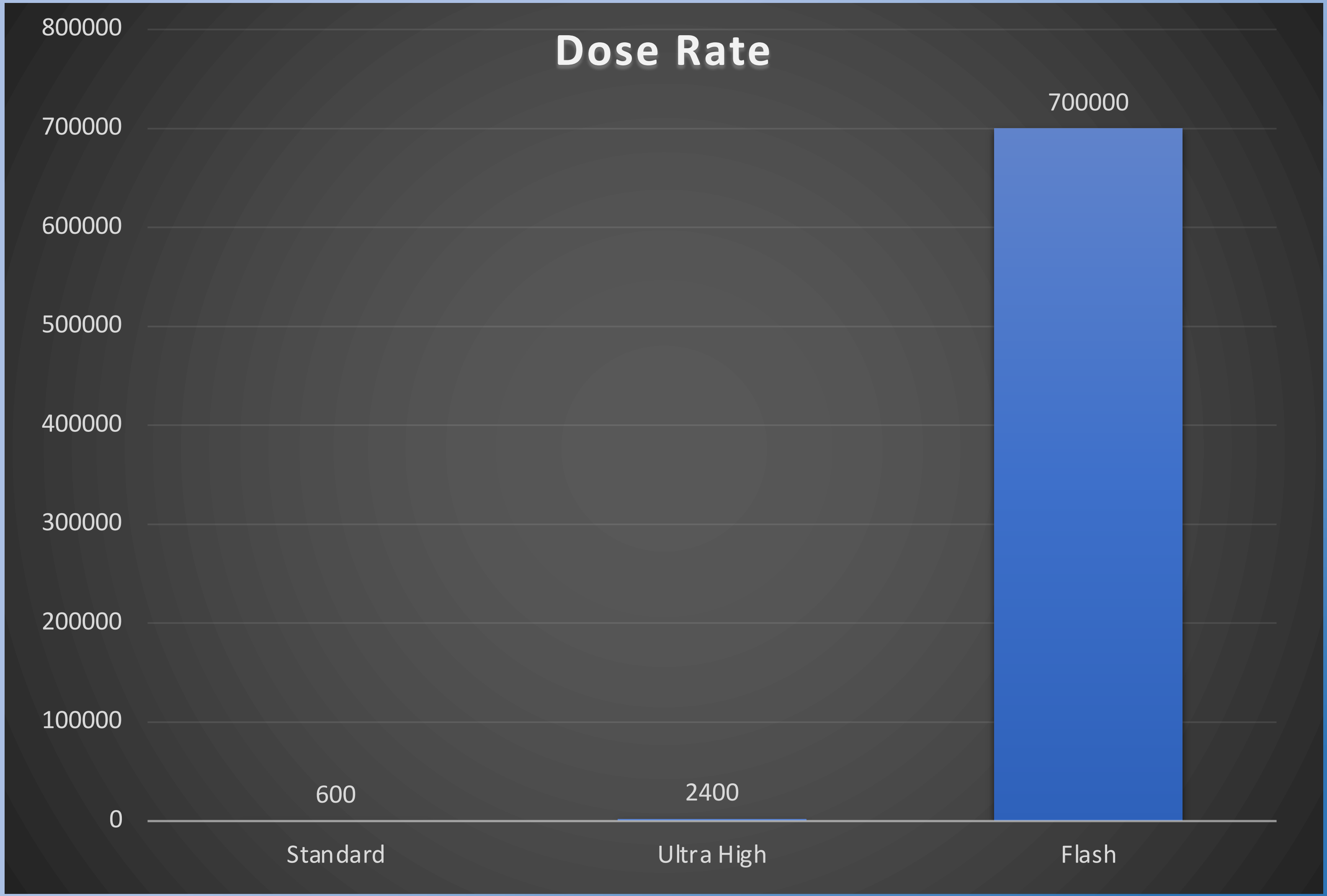


Proton minibeam radiation therapy spares normal rat brain: Long-Term Clinical, Radiological and Histopathological Analysis

Yolanda Prezado[1], Gregory Jouvion[2], David Hardy[2], Annalisa Patriarca[3], Catherine Nauraye[3], Judith Bergs[1], Wilfredo González[1], Consuelo Guardiola[1], Marjorie Juchaux[1], Dalila Labiod[4,5], Remi Dendale[3], Laurène Jourdain[6], Catherine Sebrie[6] & Frederic Pouzoulet[4,5]

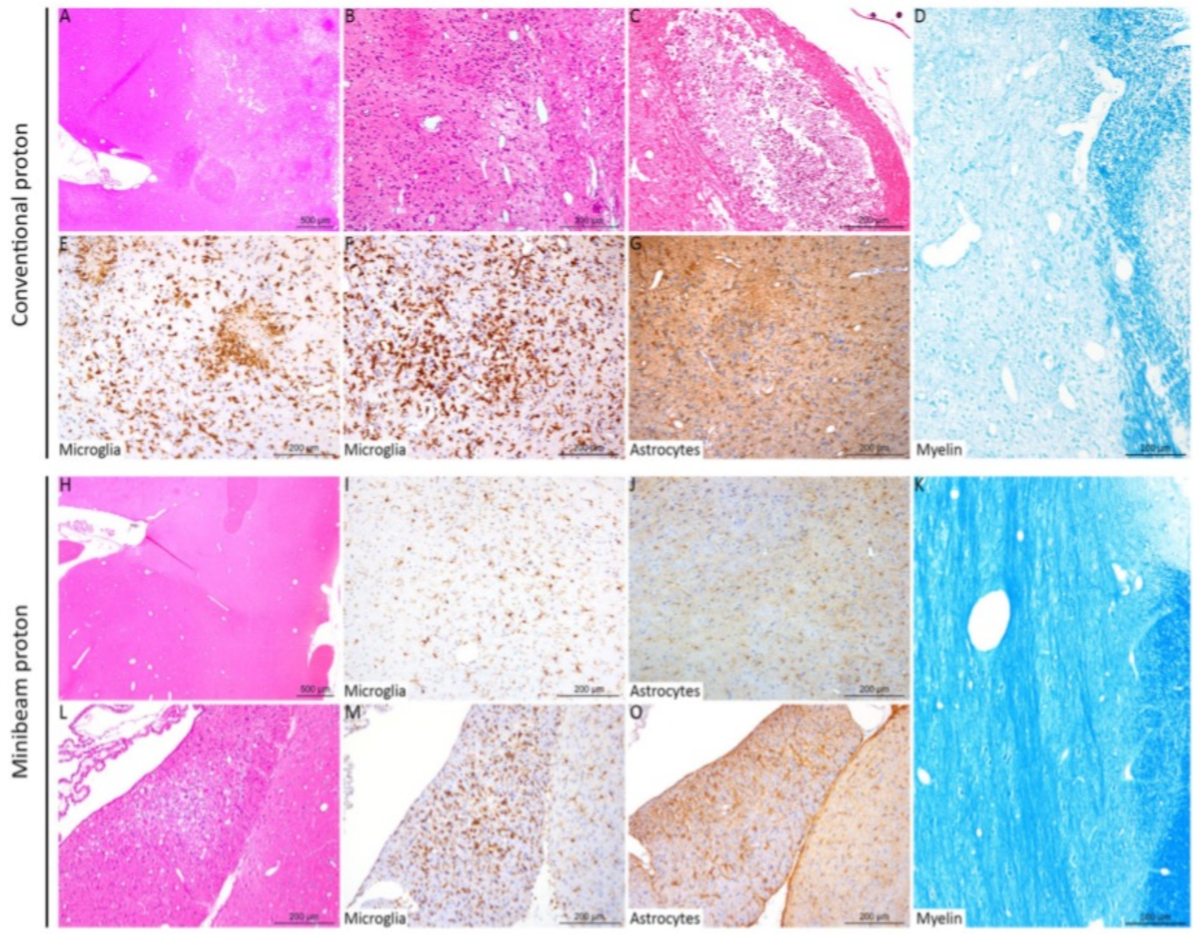
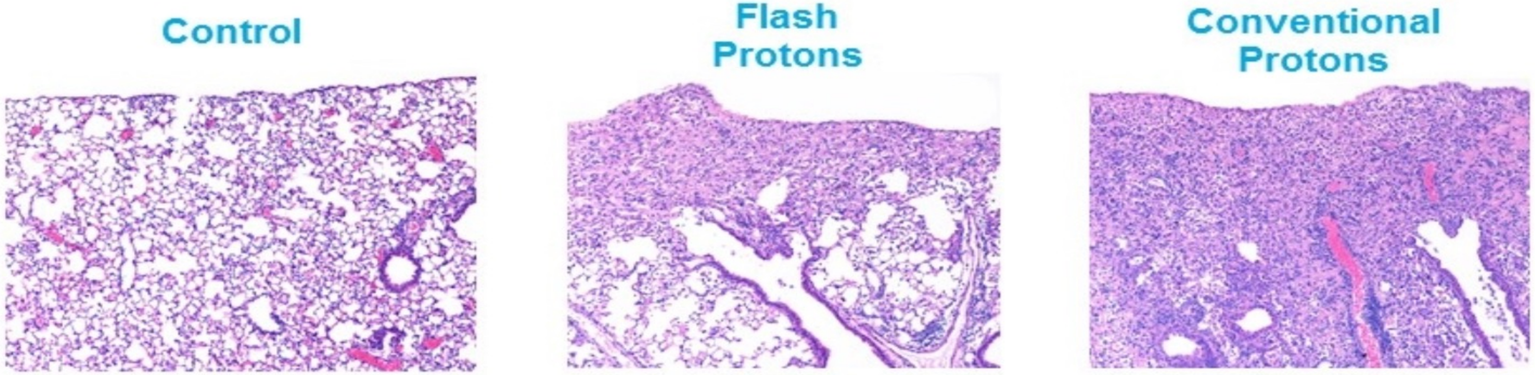


Figure 3. Histopathological and immunohistochemical analyses revealed different lesion profiles between the conventional (A–F) and minibeam (G–L) irradiation groups. A, B, C, H and L: HE staining. D and K: Luxol Fast Blue staining. E, F, I and M: anti-Iba-1 immunohistochemistry (microglia). G, J and O: anti-GFAP immunohistochemistry (astrocytes). The rats were 32 weeks old when sacrificed. Conventional irradiation: (A) Multifocal to coalescing lesion characterized by (B) oedema, necrosis and gliosis. (C) More severe lesion with cavitation and mineralisation. (D) Destruction of the myelin was also observed. (E,F) Microglial activation and microglial nodules (microgliosis). (G) Astrocyte activation with a marked increase in the GFAP immunolabeling (astrogliosis). Minibeam irradiation: (H) At low magnification, no lesion was observed in most rats, with (I,J) normal microglial and astrocytic networks, and (K) normal myelin organization. For just one rat: (L) One inflammatory infiltrate and mild neuropil destruction was observed, associated with focal (M) microgliosis and (O) astrogliosis.

Flash resulted in a reduction in radiation induced dermatitis and fibrosis

Normal tissue toxicity studies

25% reduction in fibrosis* with FLASH vs. Conventional (17.5 Gy)



35% reduction in dermatitis* with FLASH vs. Conventional (17.5 Gy)

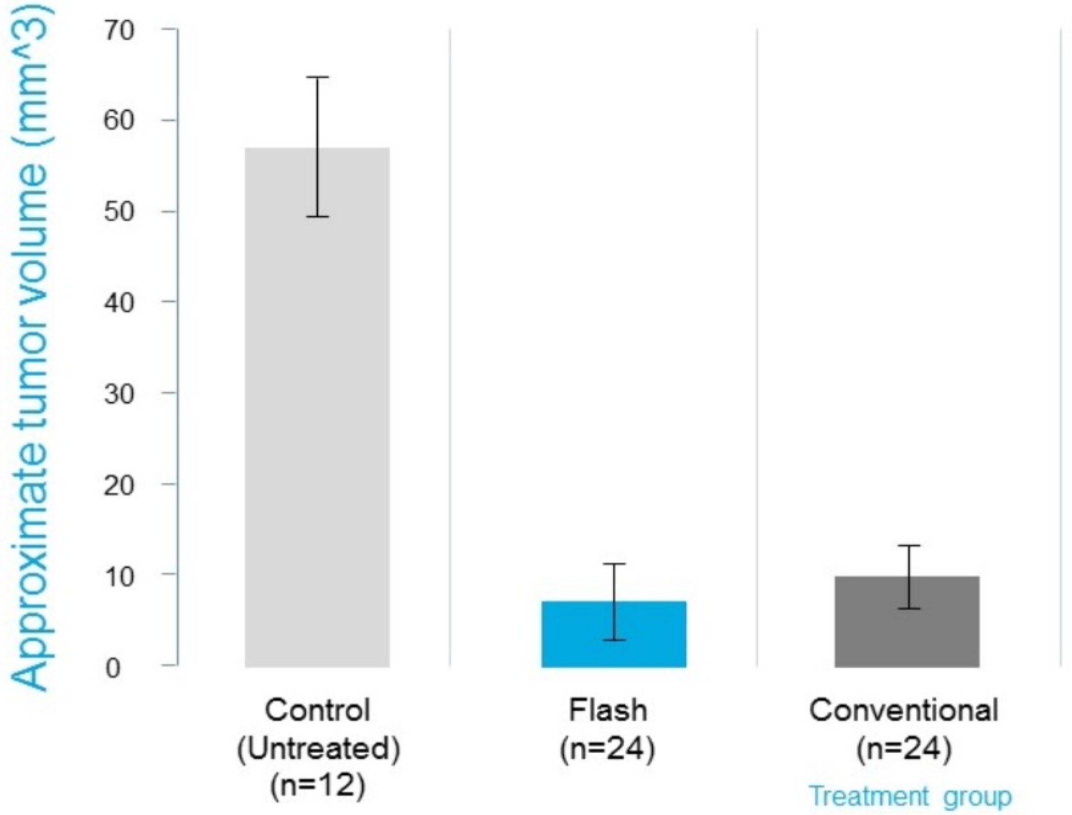
*Average dermatitis scores

LUNG FIBROSIS

(Graded by independent pathologist, blinded on treatment groups)

DERMATITIS

Tumor control preliminary results:
Proton FLASH vs Proton Conventional vs No RT



Cincinnati
Proton Therapy Center

Tumor control was the same or better with Flash compared to conventional dose rate

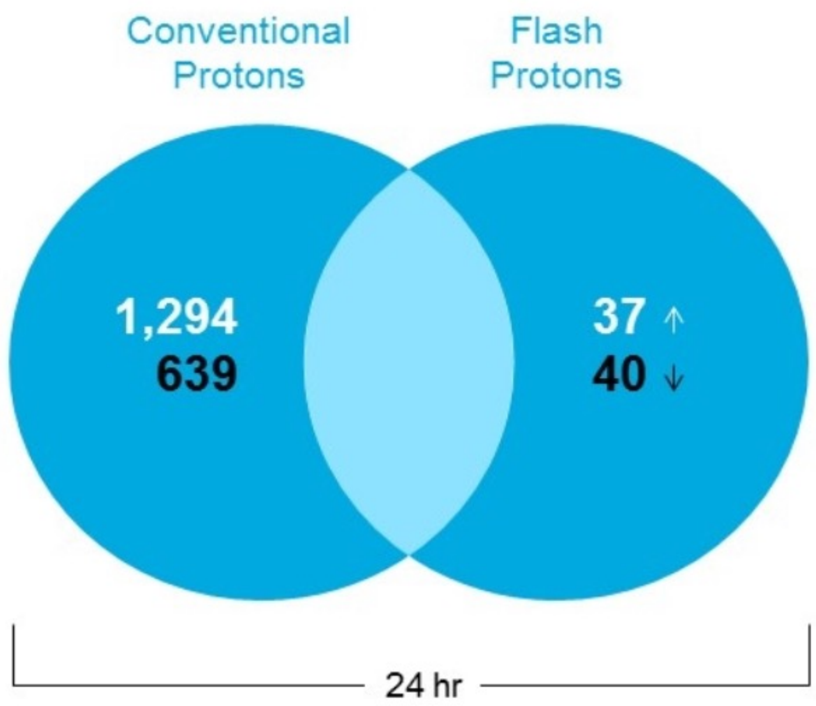
Lung Ca

Flash reduces differential gene expression normally observed with radiation therapy

Different genes are up or down regulated when comparing treatment groups versus the (untreated) control group.

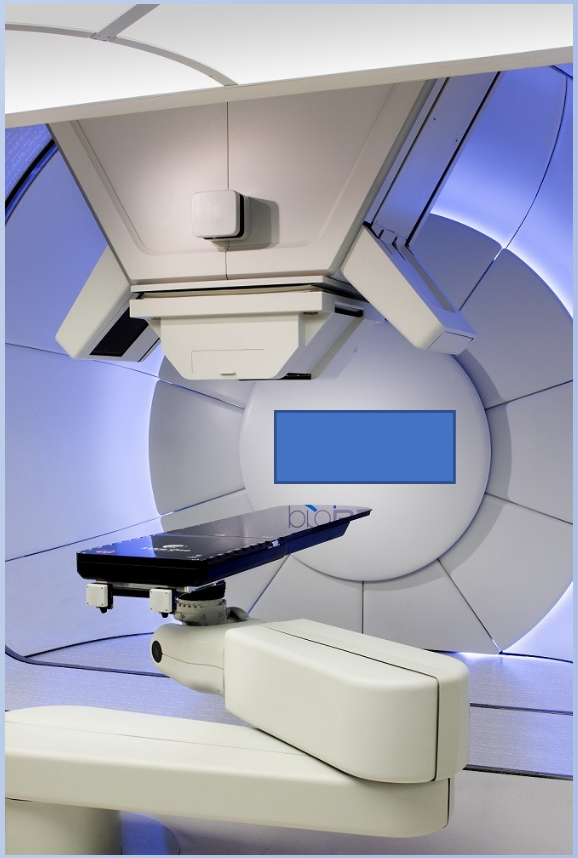
FLASH Protons have a gene expression profile closer to the (untreated) control group.

Normal Lung Tissue



Up-regulated genes
Down-regulated genes

FlashForward™ Consortium



The founding members of the FlashForward Consortium are:

- University of Maryland Department of Radiation Oncology
- Cincinnati Children's/UC Health Proton Therapy Center
- Danish Centre for Particle Therapy
- Holland Proton Therapy Centre
- New York Proton Center
- Penn Medicine
- The Christie Proton Therapy Centre
- University College London
- Proton International at the University of Alabama at Birmingham
- Emory Proton Therapy Center
- Paul Scherrer Institute
- Sylvester Comprehensive Cancer Center Proton Therapy
- VU University Medical Center Amsterdam
- South Florida Proton Therapy Institute

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Thank You!!