Current Status of Particle Therapy in Europe and beyond

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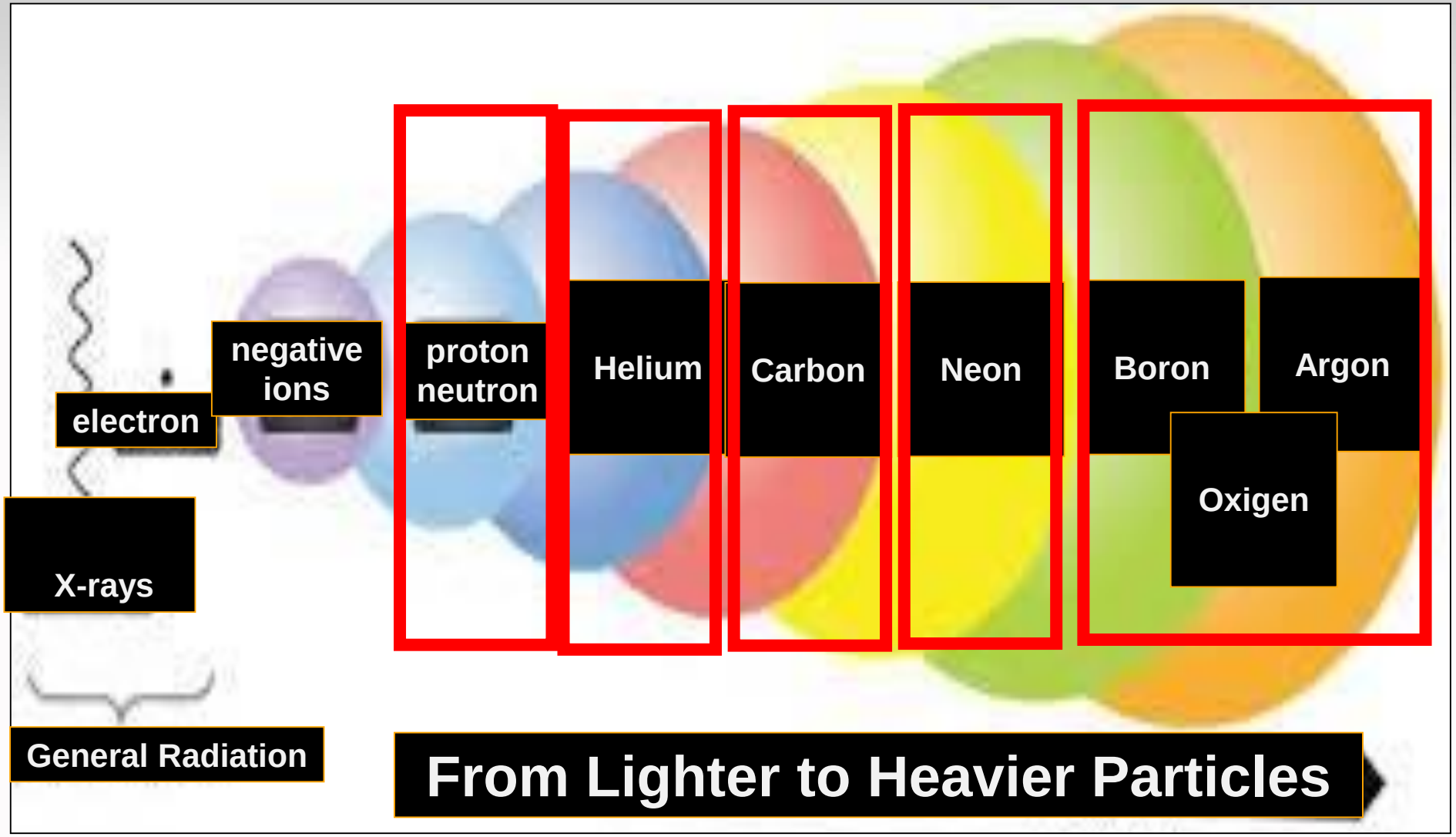
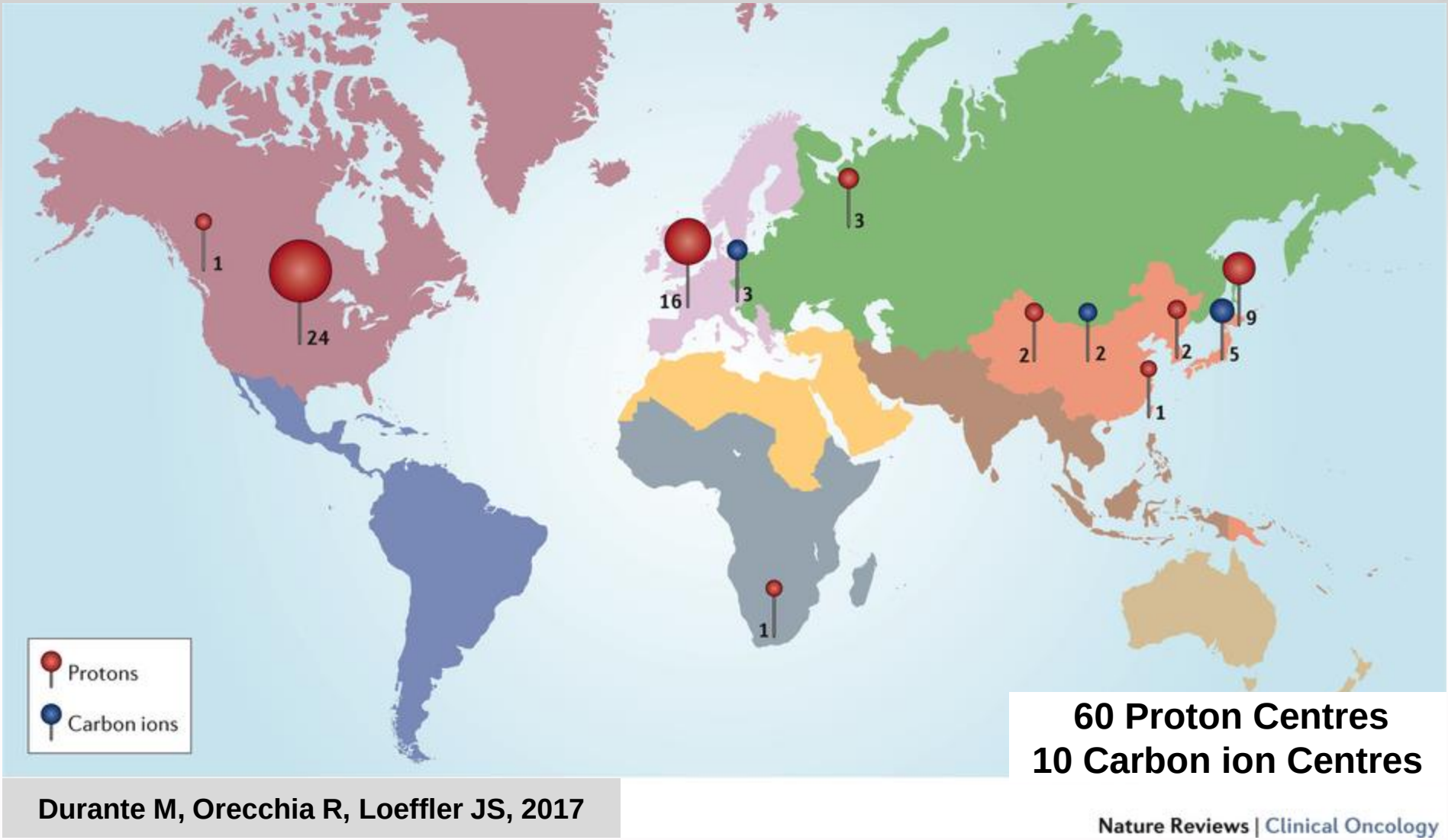
ENLIGHT
Annual Meeting

Aarhus
June, 13th 2017

Particle Beam Therapy (PBT)





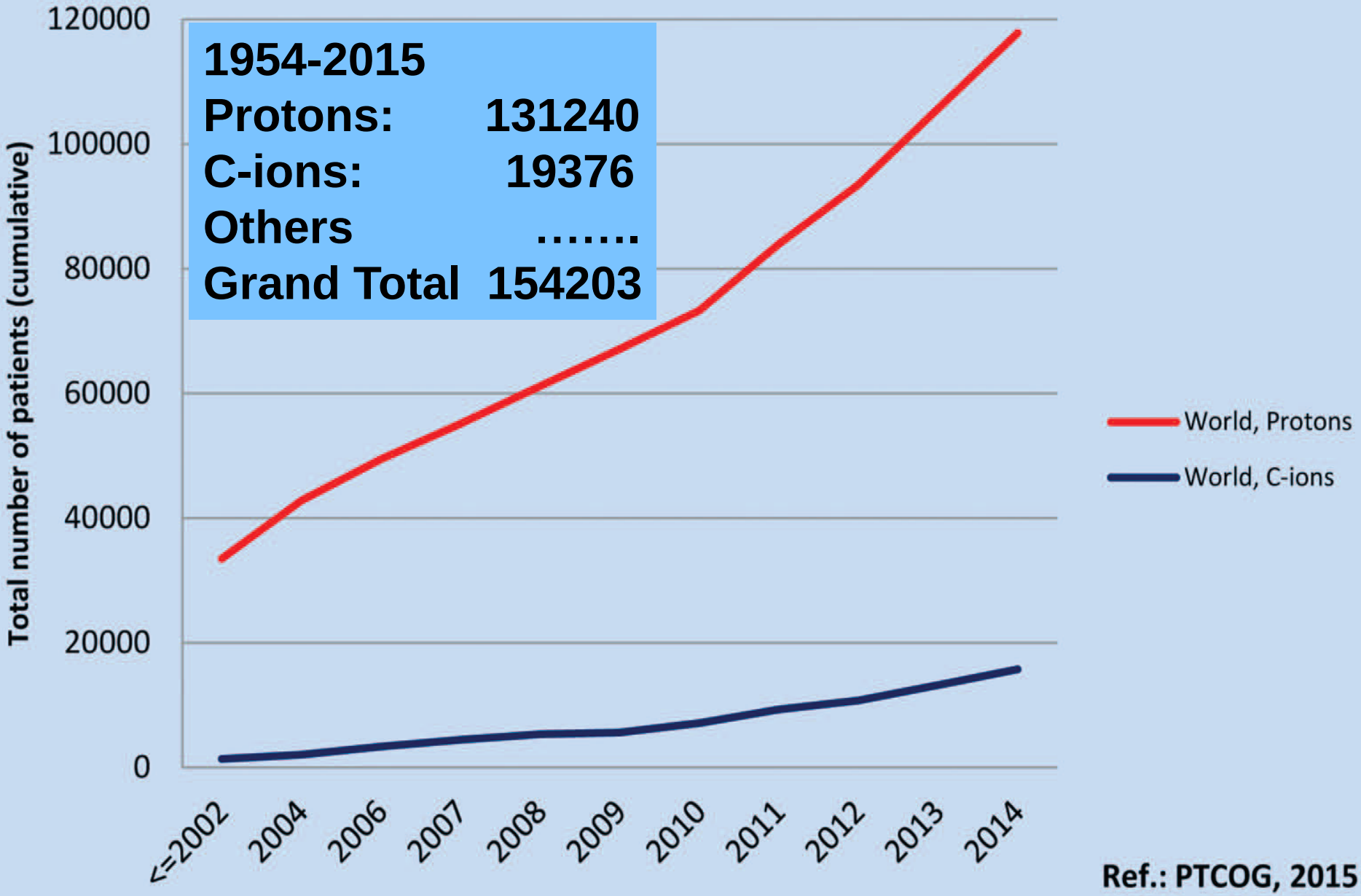
60 Proton Centres
10 Carbon ion Centres

Durante M, Orecchia R, Loeffler JS, 2017

Nature Reviews | Clinical Oncology

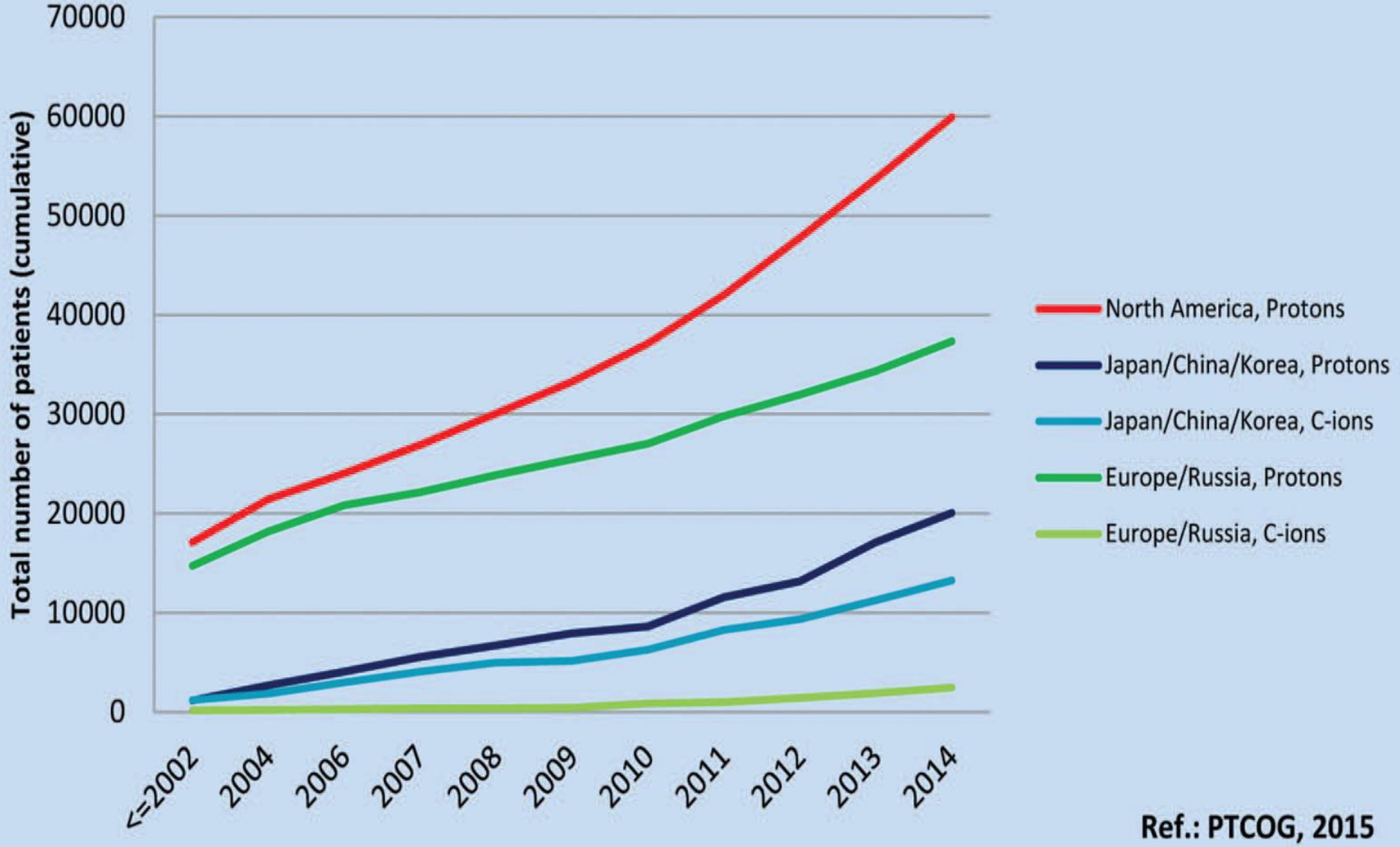
Charged Particle Therapy Centres

Patients Treated with Protons and C-ions Worldwide



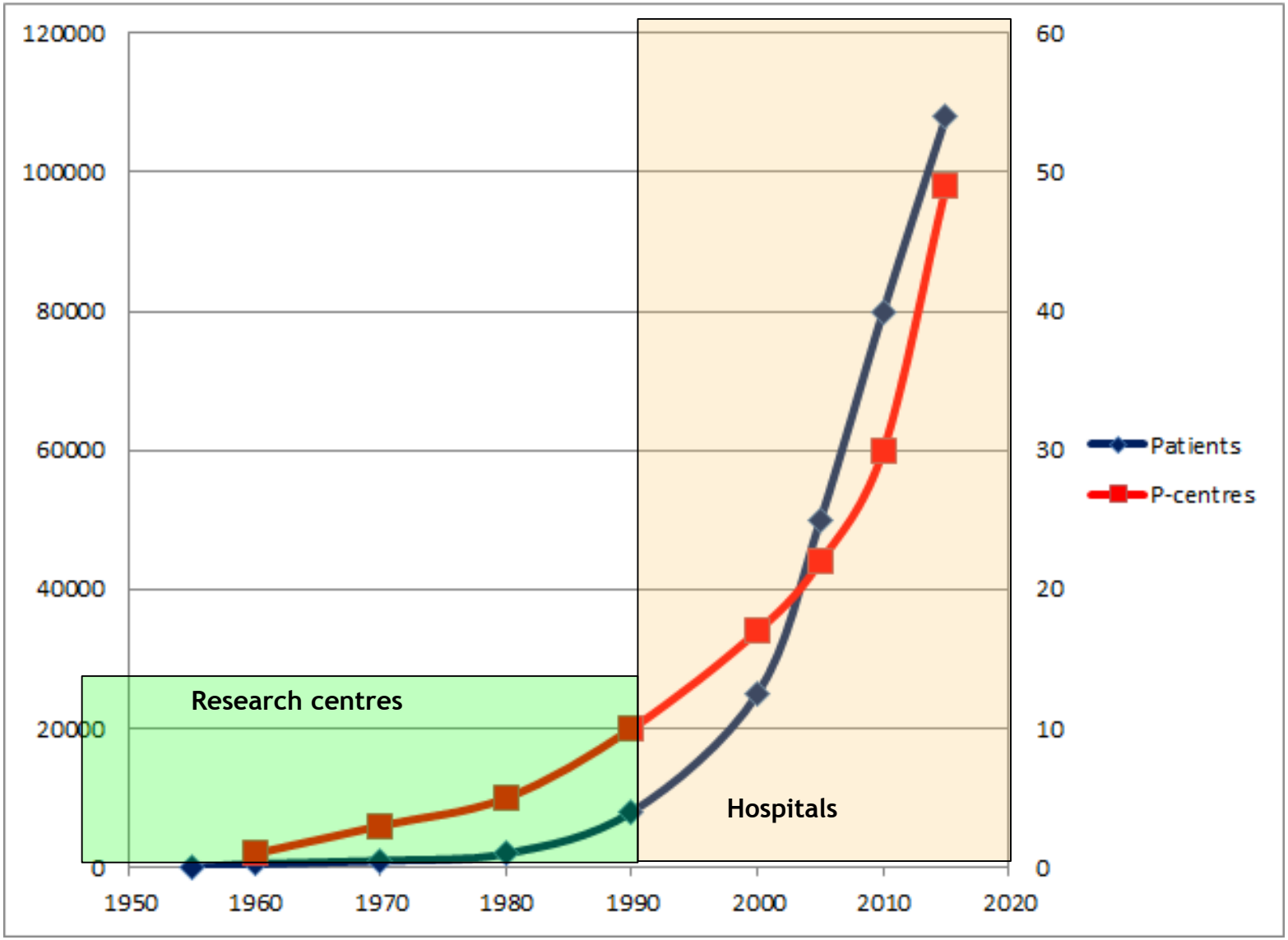
Ref.: PTCOG, 2015

Patients Treated with Protons and C-ions in North America, Asia, and Europe



Ref.: PTCOG, 2015

[Data from www.ptcog.ch]



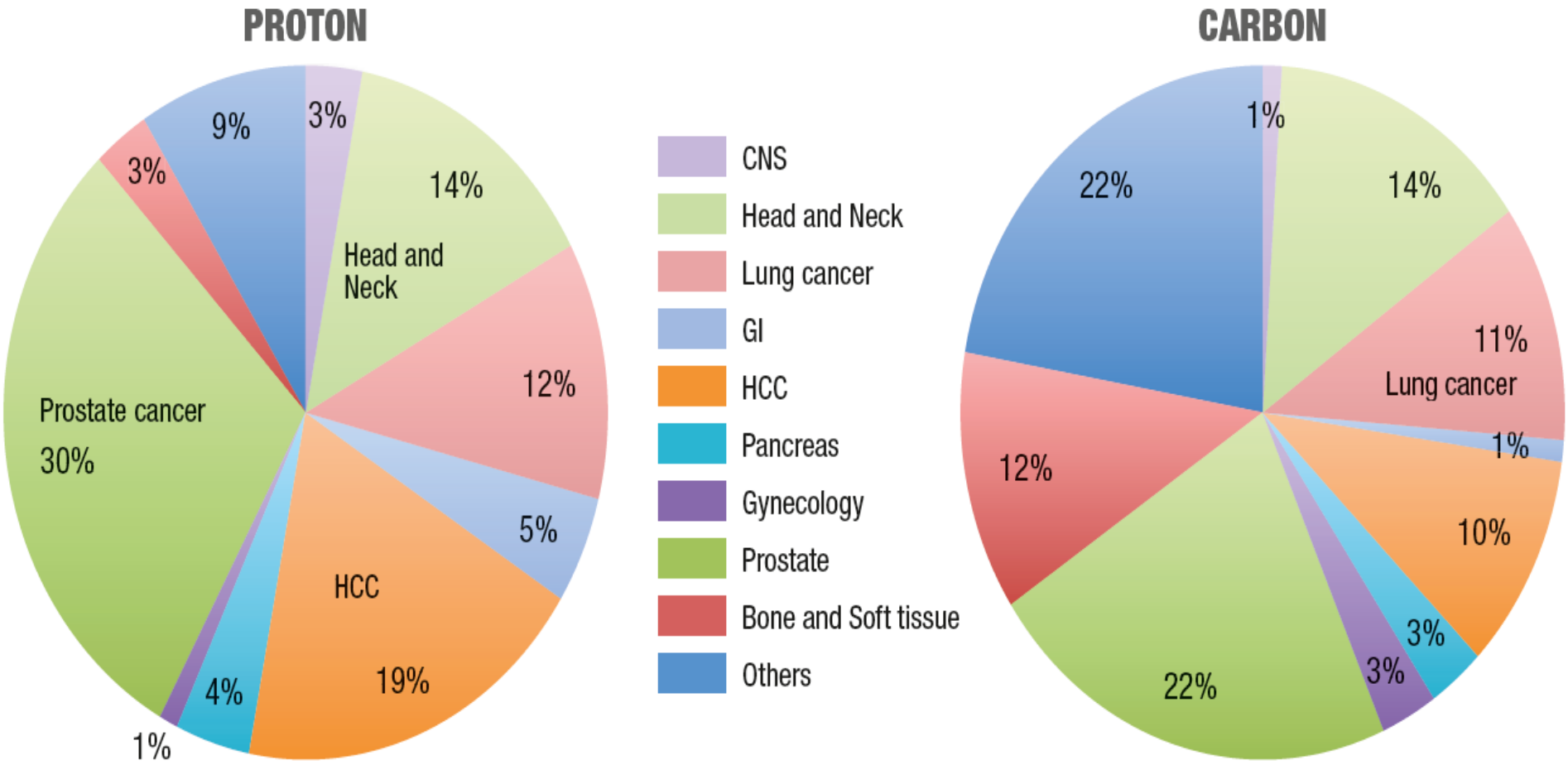
Facilities in operation (April 2017, PTCOG)

24 sites in operation
10 sites under construction
4 sites in a planning stage

Facilities in operation (April 2017, PTCOG)

15 sites in operation
4 sites under construction
1 site in a planning stage

Distribution of cases in Japan



Akimoto T et al, 2013

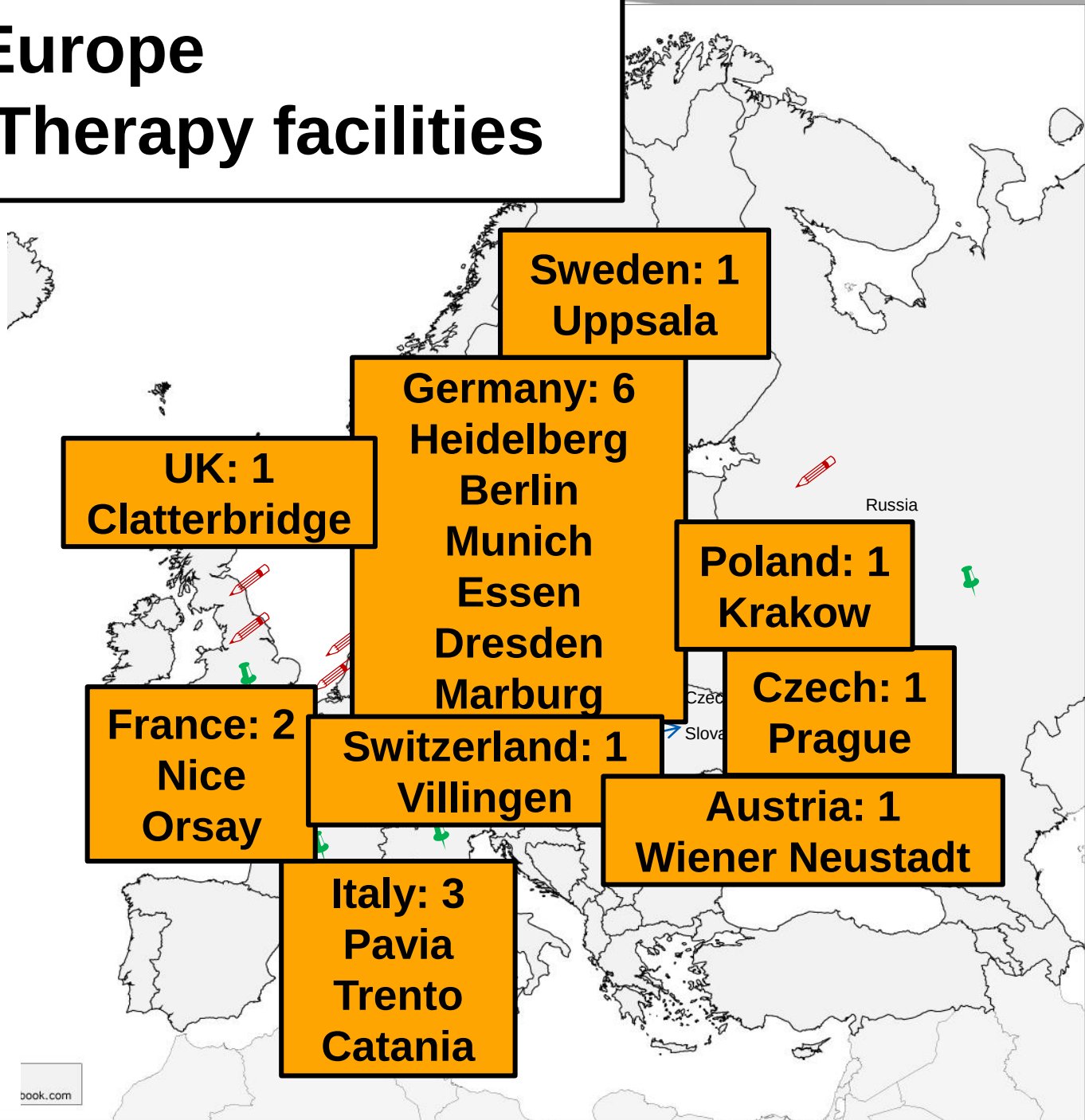
Europe
17 Particle Therapy facilities

Six centers under construction

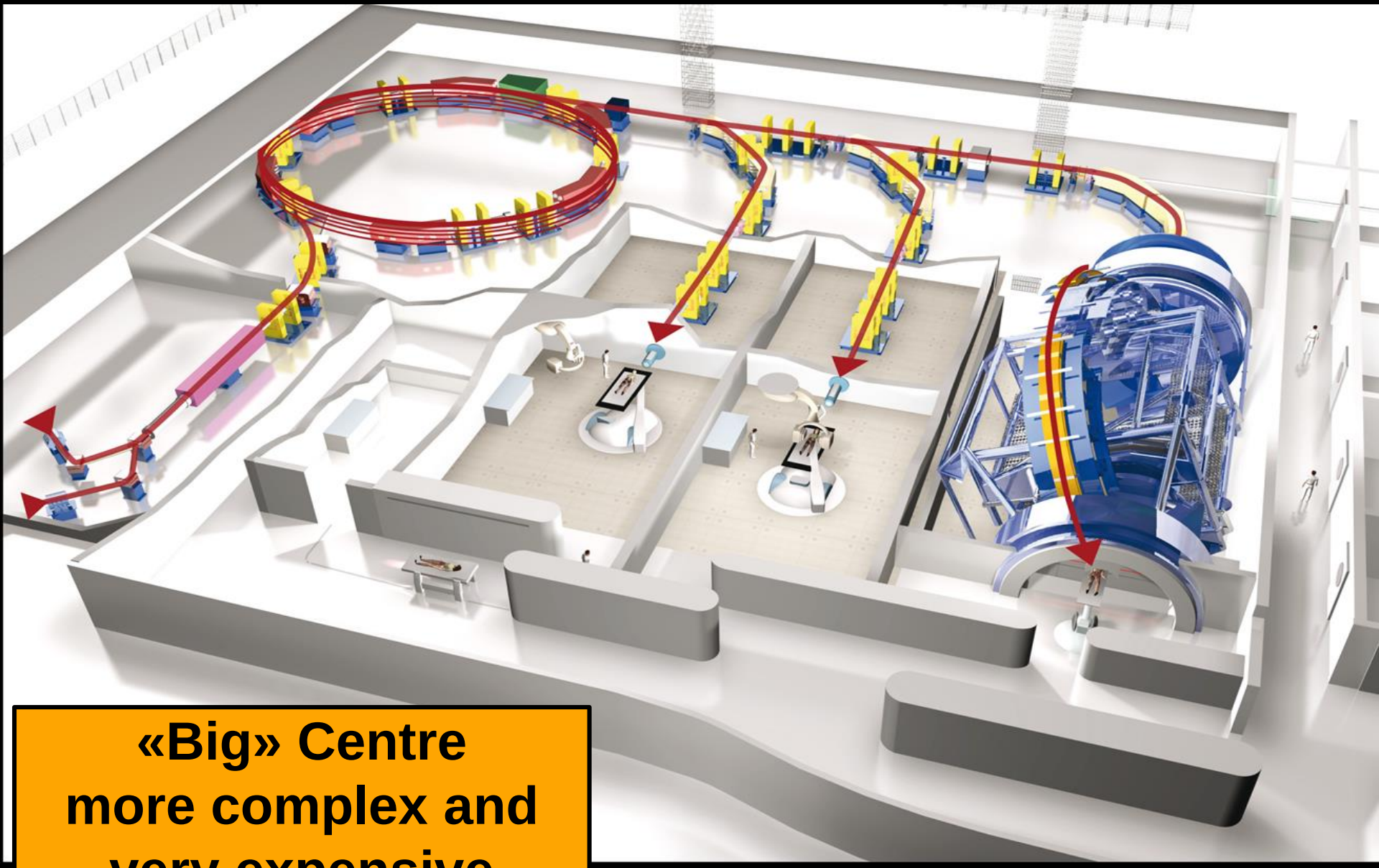
Belgium: 1
Denmark: 1
France:1
Netherland: 2
Slovak: 1

Seven centers in a planning stage

Belgium: 1
Netherland: 2
Slovak: 1
Spain: 1
Switzerland: 2



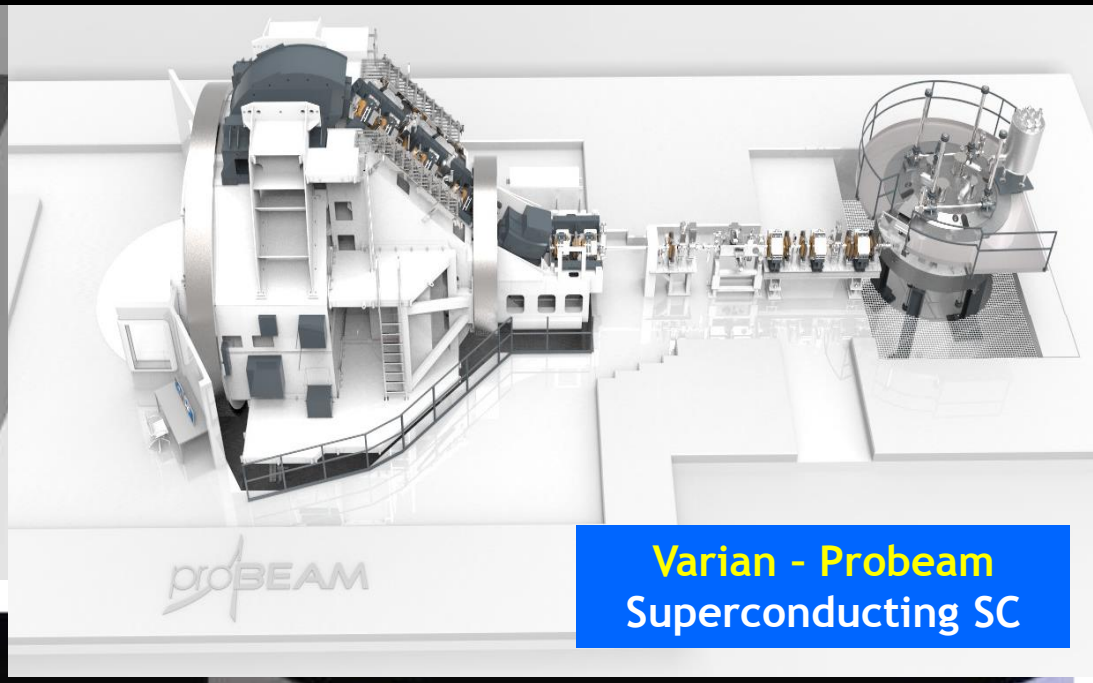
HIT - Heidelberg



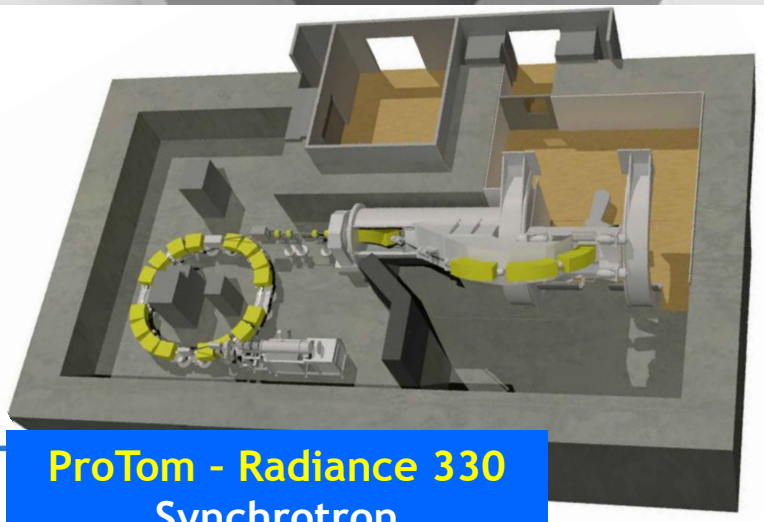
«Big» Centre more complex and very expensive

Single room facilities for protontherapy

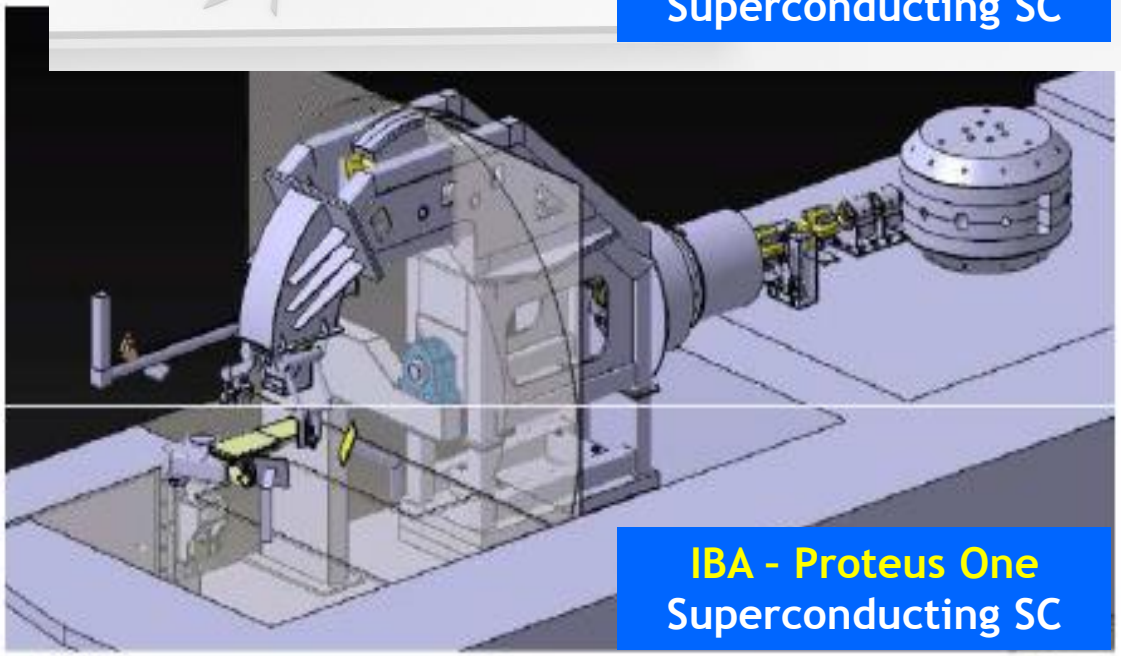
MEVION S250
Superconducting SC



Varian - Probeam
Superconducting SC



ProTom - Radiance 330
Synchrotron



IBA - Proteus One
Superconducting SC

Numbers of Cancers and Radiotherapy

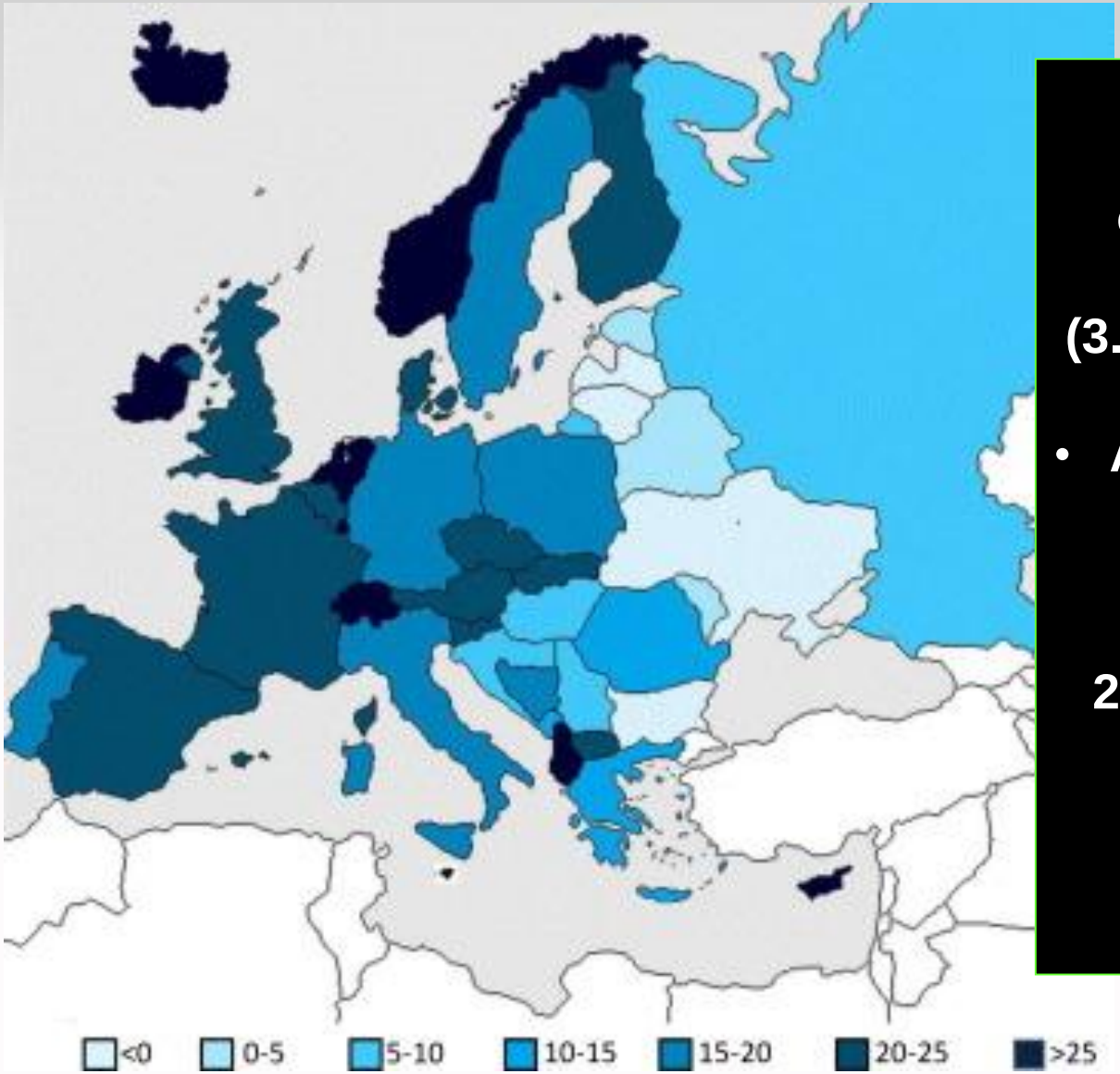
7.0 million treated by radiotherapy

- Alone or Combined
- with surgery
- with drugs
- with both

Atun R et al, Lancet Oncol 2016

Cases for RT in EU. ESTRO-HERO estimation

HERO (Health Economics in Radiation Oncology)



- About 4 million new cancer patients in Europe in 2025
(3.4 million in 2012, +15.9%)

- Absolute number of cases indicated for radiotherapy:
1.7 million in 2012
2 million in 2025 (+16.1%)

- This increases is not distributed evenly accross EU countries

Borras JM et al, Radiother Oncol 2016

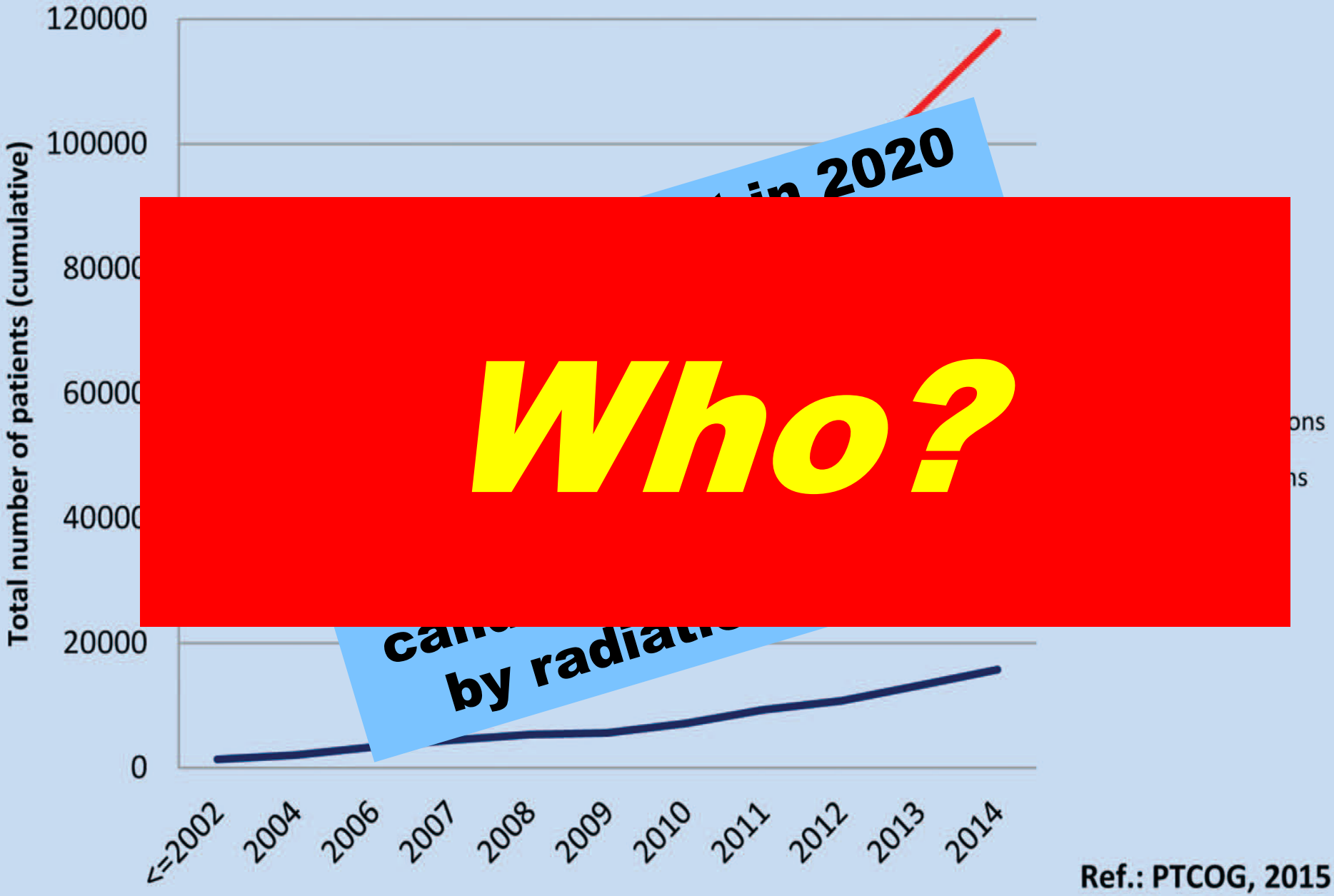
Need for RT. ESTRO-HERO estimation

Country	First	Second	Third	Fourth	Fifth
Albania	Lung	Breast	Head&Neck	Brain	Stomach
Austria	Breast	Prostate	Lung	Head&Neck	Bladder
Belarus	Breast	Lung	Head&Neck	Prostate	Rectum
Belgium	Breast	Lung	Prostate	Bladder	Head&Neck
Bosnia Herzegovina	Lung	Breast	Head&Neck		
Bulgaria	Breast	Lung	Rectum		
Croatia	Lung	Breast	Prostate		
Cyprus	Breast	Prostate	Lung		
Czech Republic	Breast	Lung	Prostate		
Denmark	Breast	Lung	Prostate		
Estonia	Prostate	Breast	Lung		
Finland	Breast	Prostate	Lung		
France	Prostate	Breast	Lung		
Germany	Breast	Prostate	Lung		
Greece	Lung	Breast	Prostate		
Hungary	Lung	Breast	Head&Neck		
Iceland	Breast	Prostate	Lung		
Ireland	Breast	Prostate	Lung		
Italy	Breast	Lung	Prostate		
Latvia	Breast	Lung	Prostate		
Lithuania	Breast	Lung	Prostate		
Luxembourg	Breast	Prostate	Lung		
Macedonia	Lung	Breast	Prostate		
Malta	Breast	Lung	Prostate		
Moldova	Lung	Breast	Head&Neck		
Montenegro	Lung	Breast	Prostate		
Norway	Prostate	Breast	Lung		
Poland	Lung	Breast	Prostate		
Portugal	Breast	Prostate	Lung		
Romania	Lung	Breast	Head&Neck		
Russian Federation	Breast	Lung	Prostate		
Serbia	Lung	Breast	Prostate		
Slovakia	Breast	Lung	Prostate		
Slovenia	Lung	Prostate	Breast		
Spain	Lung	Breast	Prostate	Rectum	Head&Neck
Sweden	Prostate	Breast	Lung	Rectum	Lymphoma
Switzerland	Prostate	Breast	Lung	Lymphoma	Head&Neck
The Netherlands	Breast	Lung	Prostate	Rectum	Lymphoma
Ukraine	Breast	Lung	Head&Neck	Rectum	Prostate
United Kingdom	Breast	Lung	Prostate	Lymphoma	Rectum
Global	Breast	Lung	Prostate	Head&Neck	Rectum

Tumor site	RT courses 2012	Increase in number 2025	Increase in rate (%)
Breast	396,891	40,524	10.2
Lung	315,197	56,558	17.9
Prostate	243,669	59,493	24.4
Head & Neck	108,194	13,337	12.3
Rectum	99,493	18,314	18.4
Lymphoma	74,852	9871	13.3
Others	……	……	……
Total	1,700.000	2,000.000	16.1%

Borras JM et al, Radiother Oncol 2016

Patients Treated with Protons and C-ions Worldwide



Ref.: PTCOG, 2015

ASTRO point of view

- **Evidence for large ocular melanomas, chordomas and chondrosarcomas**
- **« A suggestion » for pediatric CNS malignancies**
- **Efficacy but not superiority for HCC and prostate**
- **No evidence for lung, H&N, GI, and pediatric non-CNS malignancies**

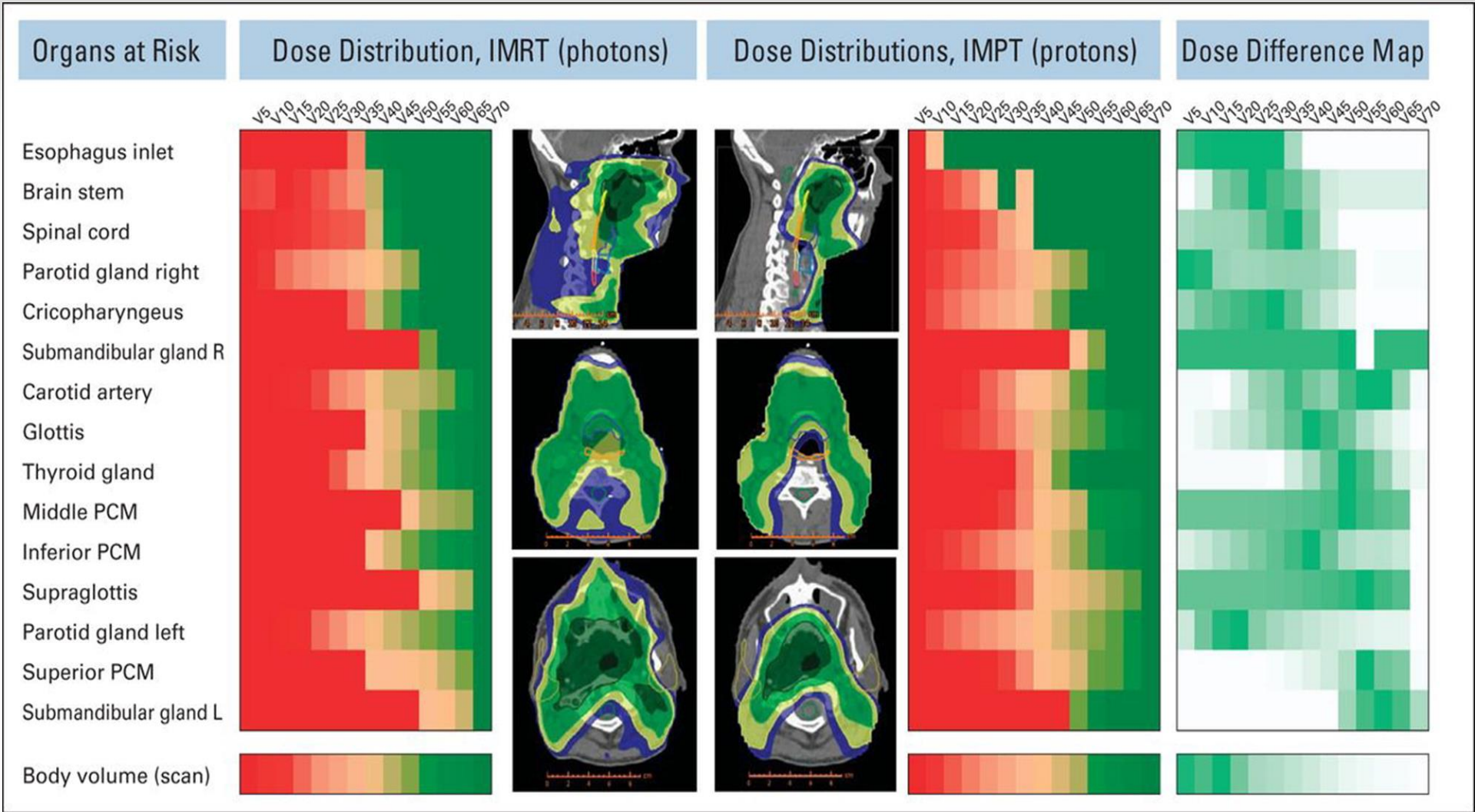
Allen AM et al, Radiother Oncol 2012

- **PBT « is considered reasonable in instances where sparing the surrounding normal tissue cannot be adequately achieved with photon-based RT and is of added clinical benefit to the patient »**

PBT, ASTRO Model Policies, 2014

Dutch Model

TCP and NTCP comparison



Italian Model - LEA in NHS

1. Chordoma & chondrosarcoma base/spine
2. Meningiomas
3. Brain tumors (trunk)
4. ACC Salivary Glands
5. Orbit tumors including eye melanoma
6. Sinonasal carcinoma
7. Soft Tissue & bone Sarcoma (every sites)
8. Recurrent tumors (retreatment)
9. Patients with immulogical desorders
10. Pediatric solid tumors

2017

Italian Model - LEA in NHS

Conditions for prescription

Patients with a tumor as listed, without metastases, PS ECOG 0-2, absence of concomitant disease or comorbibity at risk to significant decrease of life expentancy

Reimbursement

1. Full cycle (24,000 E)
2. Boost (up to 6 fractions) (12,000 E)
3. Stereotactic treatment (1 to 3 fractions) (18,000 E)

Cost-Effectiveness

The large benefit in C-E is on pediatric brain tumours

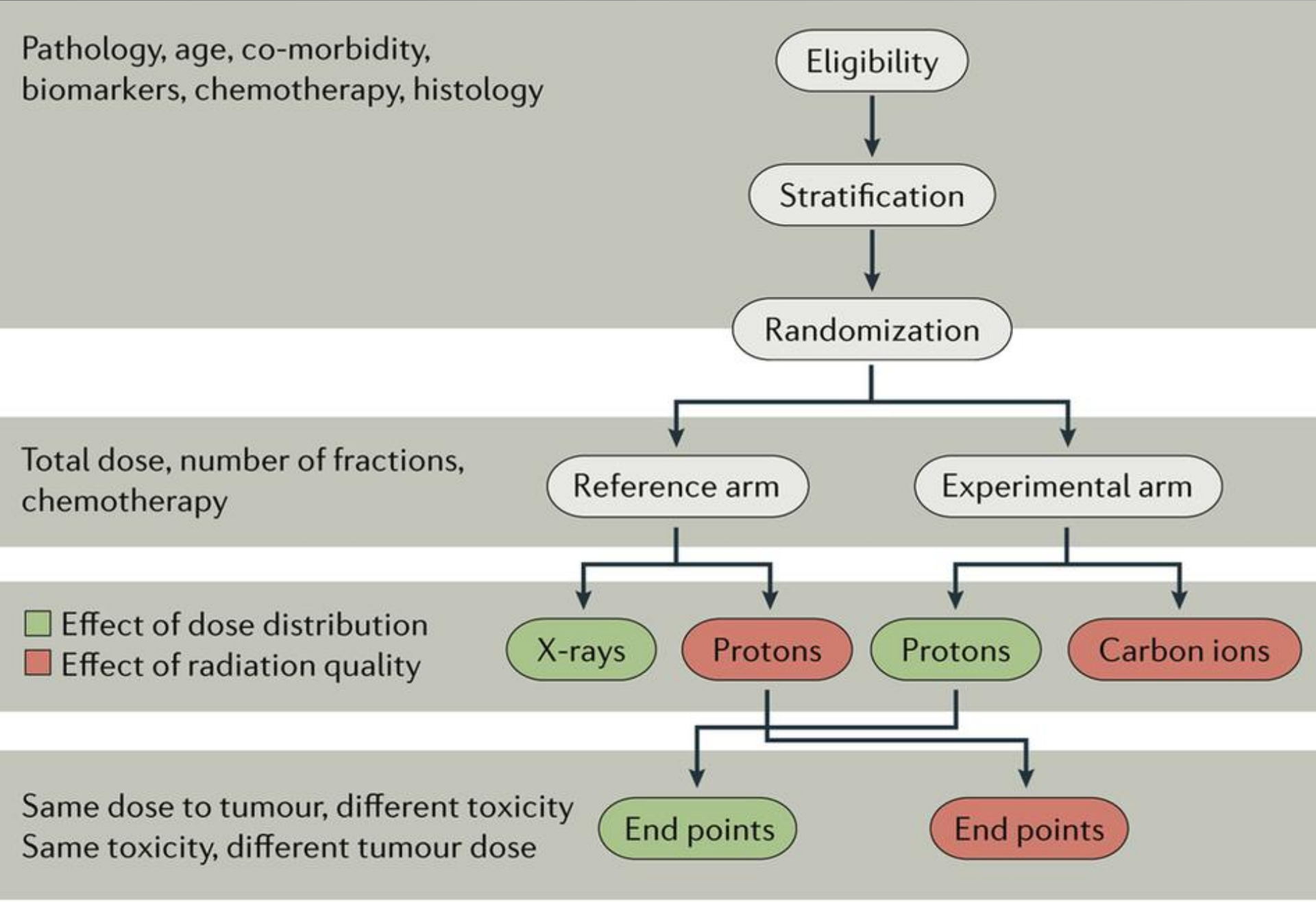
PBT offered superior C-E in selected H&H cancer (toxicity), breast (left-sided), NSCLC (only advanced), eye melanoma

It is highly unlikely that PBT will be the most economic option for all or even for all patients with a given type of cancer

Rather, the major goal for ongoing and future research will be to identify the subpopulation(s) of each cancer type for whom PBT is most C-E

Verma V et al, Cancer 2016

nd
Trials



Durante M, Orecchia R, Loeffler JS, 2017

Nature Reviews | Clinical Oncology

P+ ongoing randomized trials

Study	Institution	Condition
R03CA188162 IMPT versus IMRT	MDACC Houston	Oropharynx
NCT01617161 P+ versus IMRT	MGH Boston	Low Risk & Intermediate Risk prostate
NCT01512589 IMPT versus IMRT	MDACC Houston	Oesophagus
RADCOMP (NCT02603341) P+ versus X-rays	Penn University	PMRT stage II-III breast
NRG 1542 P+ versus SBRT	NRG Oncology	Hepatocellular
PO1CA021239-29 A1 P+ versus IGRT (+CT)	MDACC/MGH	Locally advanced (II/III) SCC Lung
RTOG 1308	RTOG	Inoperable (IIIB) SCC lung

Durante M, Orecchia R, Loeffler JS, 2017

C-12 ongoing randomized trials

Study	Institution	Condition
NCTO1182753 p+ versus C-12	Heidelberg	Skull base low- and intermediate-grade chondrosarcoma
NCTO1182779 p+ versus C-12	Heidelberg	Skull base Chordoma
ETOILE NCTO2838602 C-12 versus IMRT	Lyon/CNAO /HIT	H&N adenoid cystic carcinoma and sarcomas
BAA-N01CM51007-51 C-12 versus IMRT	NCI/Shanghai Phase I/III	Locally advanced pancreatic cancer
CIPHER: C-12 versus IMRT (+ CT)	Dallas/NIRS/ CNAO	Locally advanced pancreatic cancer

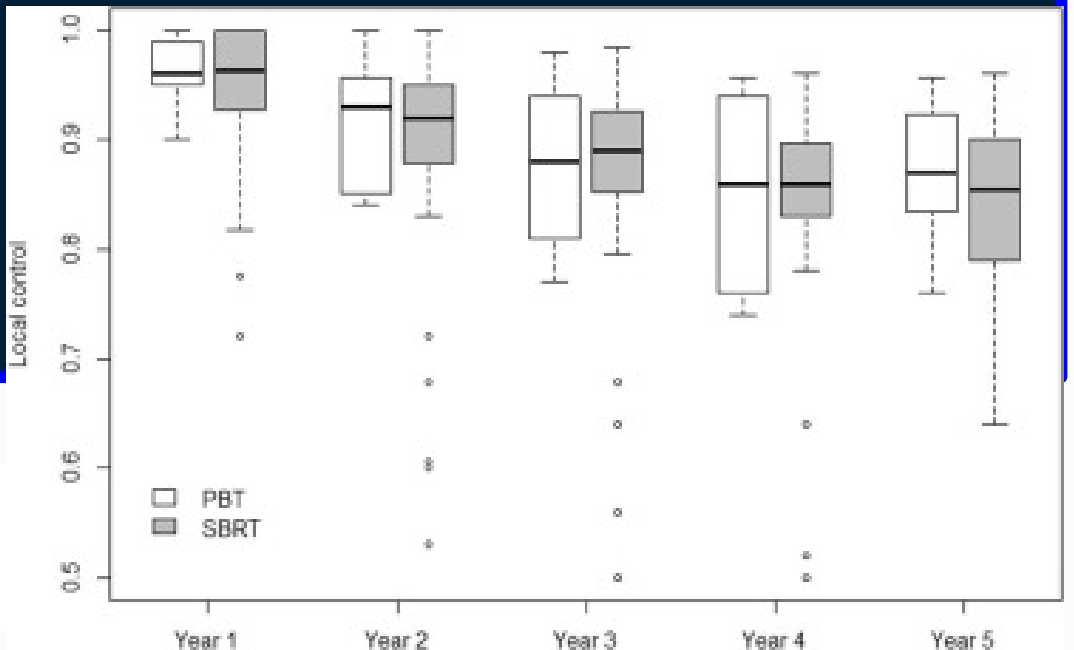
Durante M, Orecchia R, Loeffler JS, 2017

SBRT vs hypofractionated PBT

Early stage NSCLC, 2000-2016

Although HF PBT may lead to additional clinical benefit when compared with SBRT, no statistically significant survival benefit was observed (p = 0.11) after adjusting for potential confounding variables

The 3-year LC still favored PBT (p = 0.03)



Chi A et al, Radiother Oncol 2017
http://dx.doi.org/10.1016/j.radonc.2017.05.007

CNS Tumours?

- **Vestibular schwannoma**: protons inferior to photons
- **Meningiomas**: marginal improvement
- **Low-grade gliomas**: comparable results
- **High grade gliomas**: significant side effects in dose-escalation studies, thus this strategy needs to be rethought
- **Pediatric CNS tumours**: the largest benefit is considered, but long-term data are still lacking, and even recent analyses do not all lead to a clear reduction in side effects with improvement of outcome
- However, based on preclinical evidence, protons should be evaluated **in every pediatric patients**
- Protons should be evaluated for **chordoma and chondrosarcoma of the skull base**

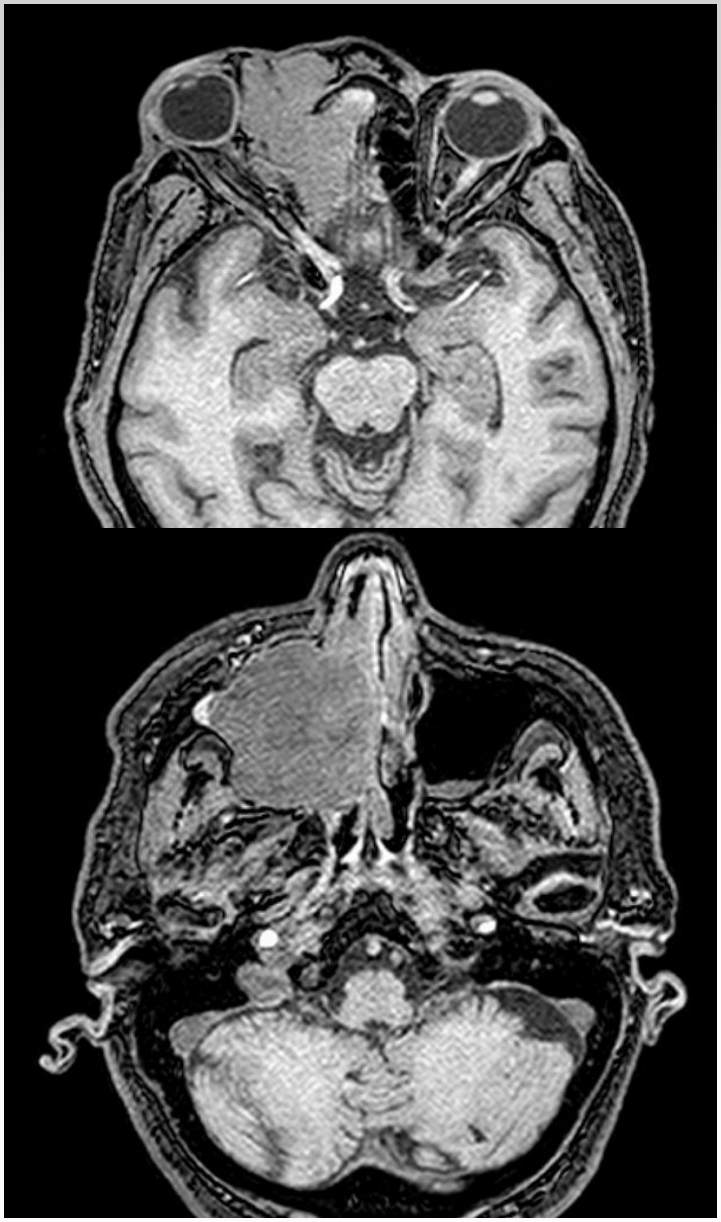
Combs SE, Curr Treat Options Neurol 2017

PBT – Present and future

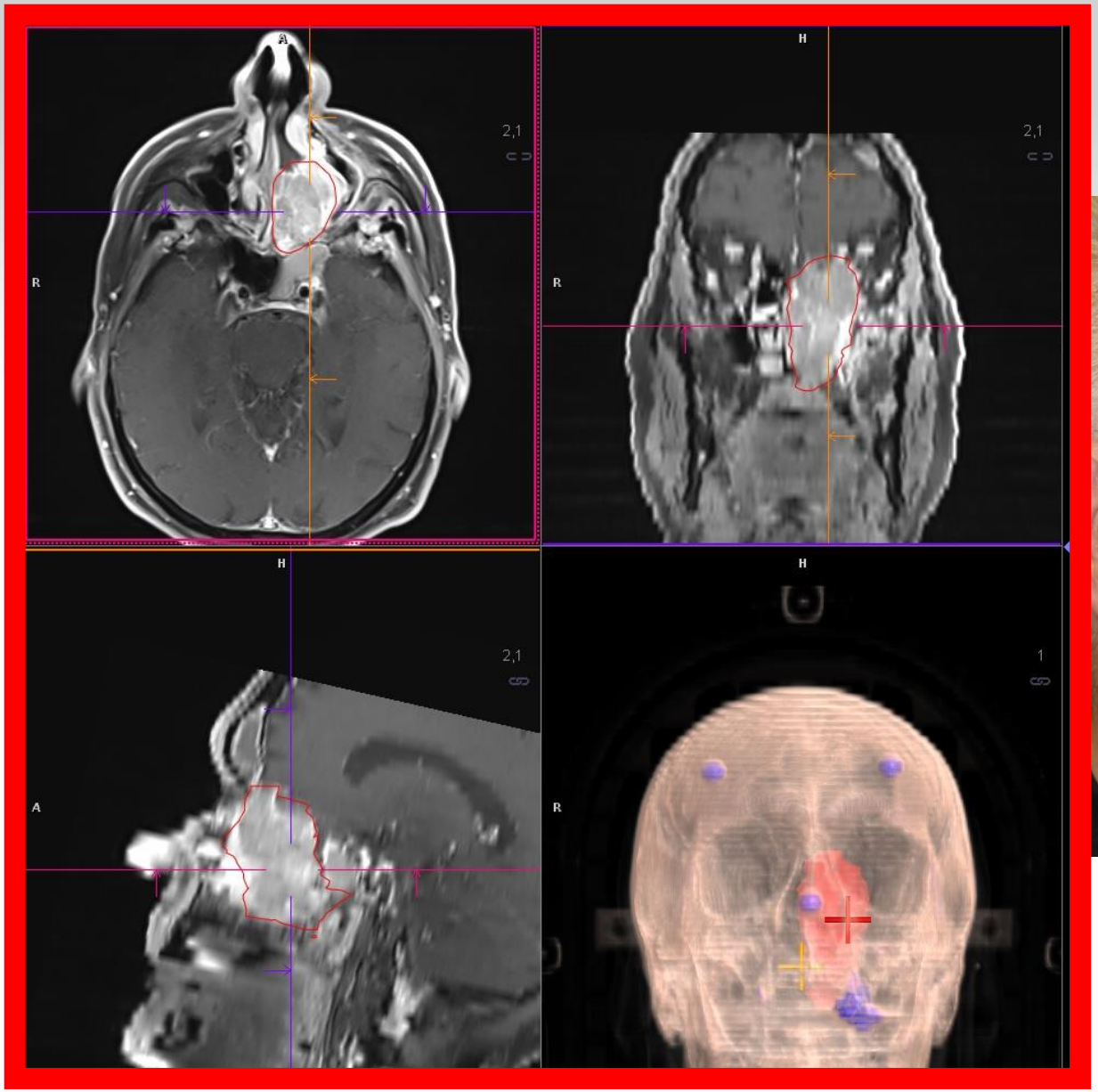
1. Physical and biological uncertainties
2. Optimization and robustness of TP
3. Tecnological limitations:

- Spot size
- Energy switching
- In-Room Volumetric IG
- Respiratory gating
- Dynamic collimation
- High cost
- Particles other than Protons

PBT can change the paradigm?



PBT can change the paradigm?




Molecular Imaging
& Biology driven
studies
In the future, we could
use targeted particles
exactly as now we are
using targeted drugs .....

Thank you very much for your attention !!!!!!