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Status of Clinical Hadrontherapy in Caen And roadmap for carbon ion / multi ion therapy

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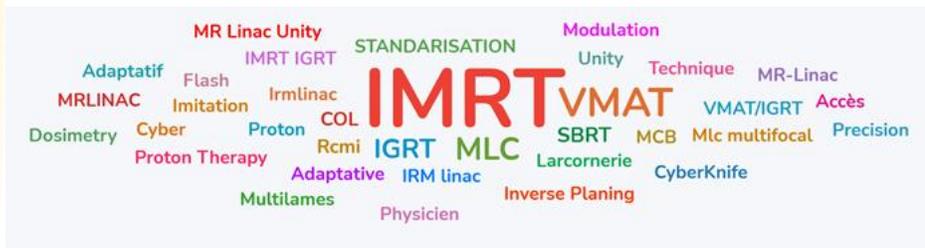


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Perception of proton therapy in France by the medical community, until recently

- 120 participants (rad oncs, phy, RTT)

The greatest success in radiotherapy over the past three decades



What has been the greatest failure of radiotherapy over the past 30 years?



- Insufficient **level of evidence**? Too slow
- Some unexplained toxicities?
- Difficult patient referral pathways? treatment **delays**?
- Health economics : **Cost**?
- Cognitive bias?





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Evidence from the US == > Change in practice trial in head and neck cancer in 2025

- Frank SJ Lancet 2025
- Better progression-free survival and overall survival
- Less toxicities

	Intensity-modulated (photon) radiation therapy (n=136)			Intensity-modulated proton therapy (n=160)		
	Grade 3	Grade 4	Grade 5	Grade 3	Grade 4	Grade 5
Lymphopenia	75 (55%)	46 (34%)	0	103 (64%)	18 (11%)	0
Oral mucositis	60 (44%)	2 (2%)	0	65 (41%)	0	0
Dysphagia	67 (49%)	0	0	54 (34%)	0	0
Oral pain	32 (24%)	0	0	39 (24%)	0	0
Weight loss	75 (55%)	0	0	74 (46%)	0	0
Dermatitis radiation	25 (18%)	0	0	39 (24%)	0	0
Nausea	19 (14%)	0	0	17 (11%)	0	0
Xerostomia (dry mouth)	61 (45%)	0	0	52 (33%)	0	0
Neutropenia	9 (7%)	4 (3%)	0	3 (2%)	1 (1%)	0
Fatigue	9 (7%)	0	0	5 (3%)	0	0
Thrombocytopenia	2 (1%)	0	0	1 (1%)	0	0
Dehydration	3 (2%)	0	0	5 (3%)	0	0
Oesophagitis	3 (2%)	0	0	5 (3%)	0	0
Vomiting	3 (2%)	0	0	6 (4%)	0	0
Anaemia	2 (1%)	0	0	1 (1%)	0	0
Aspiration	1 (1%)	1 (1%)	0	0	0	0
Osteoradionecrosis	2 (1%)	0	0	1 (1%)	0	0
Suicide	0	0	2 (1%)	0	0	0

Data are n (%). Severe adverse events are defined as grade 3 or worse adverse events per the Common Toxicity Criteria Adverse Events framework. Over 95% of severe adverse events occurred during treatment or within 90 days after treatment. All patients received concurrent systemic therapy.

Table 2: Severe adverse events in the per-protocol population

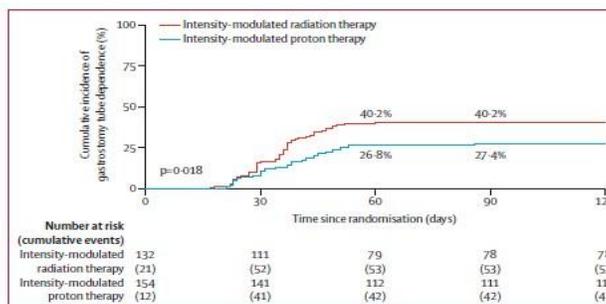
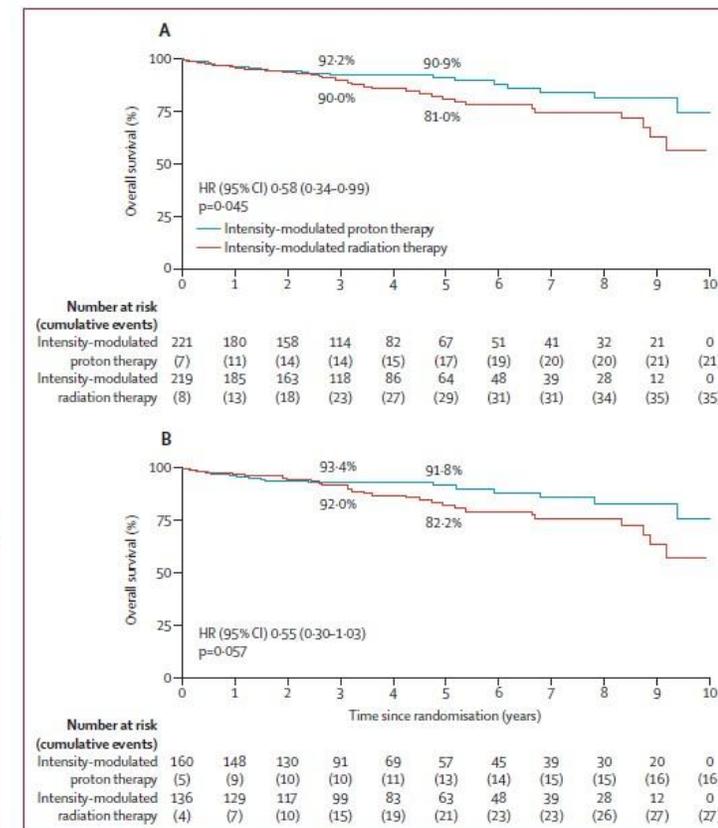
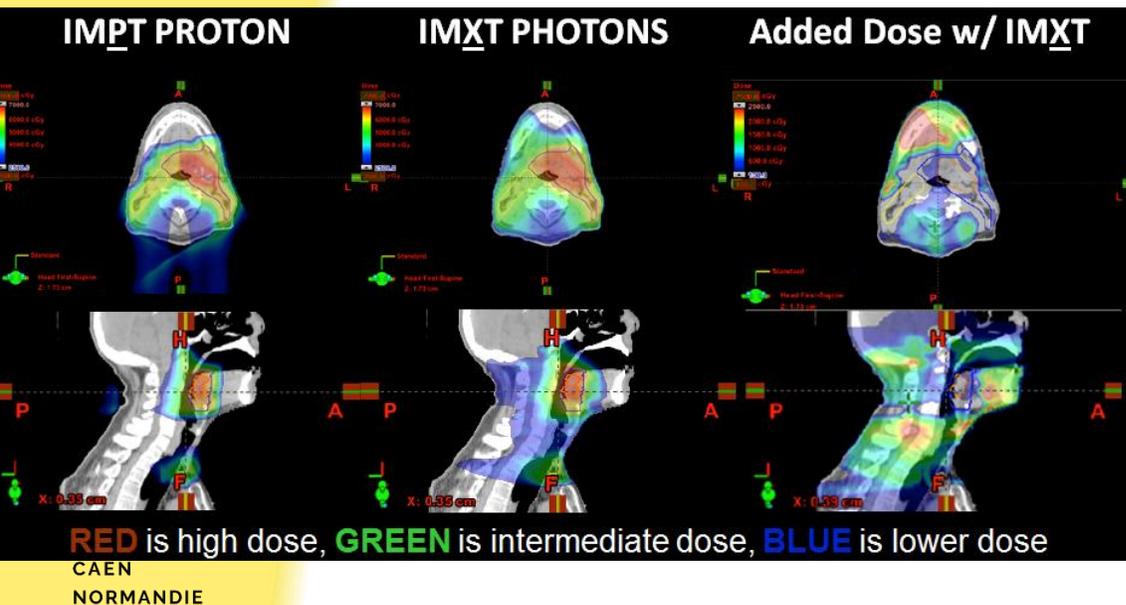


Figure 5: Cumulative incidence of gastrostomy-tube dependence in the per-protocol population. Patients with prophylactic gastrostomy tubes were excluded, four patients in the intensity-modulated radiation therapy group and six patients in the intensity-modulated proton therapy group.

Figure 3: Overall survival in the intention-to-treat population (A) and the per-protocol population (B). HR=hazard ratio.



Strategies to increase the level of evidence in France

Matched study of French healthcare utilization comparing proton and photon therapy using SNDS data



- 13,000 patients, including 4,000 treated with protons (2018 – opening of proton therapy in Caen – 2022)
- Study based on the French National Health Data System (SNDS)
- From meningiomas to radioresistant skull base and spinal tumors.
- **Referral bias toward proton therapy for patients with pre-existing sensory deficits (optic or ENT sequelae) prior to radiotherapy.**
- Despite this, survival was similar to markedly superior.
- Investigating ways to obtain data on French patients referred abroad (Germany, Italy, and other countries).



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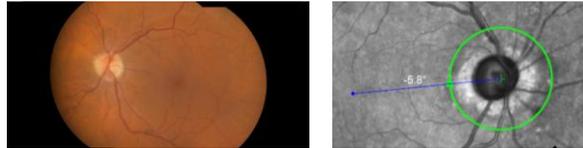
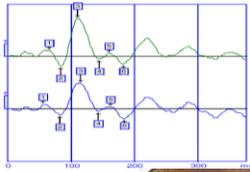


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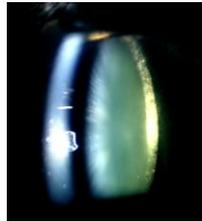
Strategies to increase the level of evidence in France

Prospective multi-scale cohorts

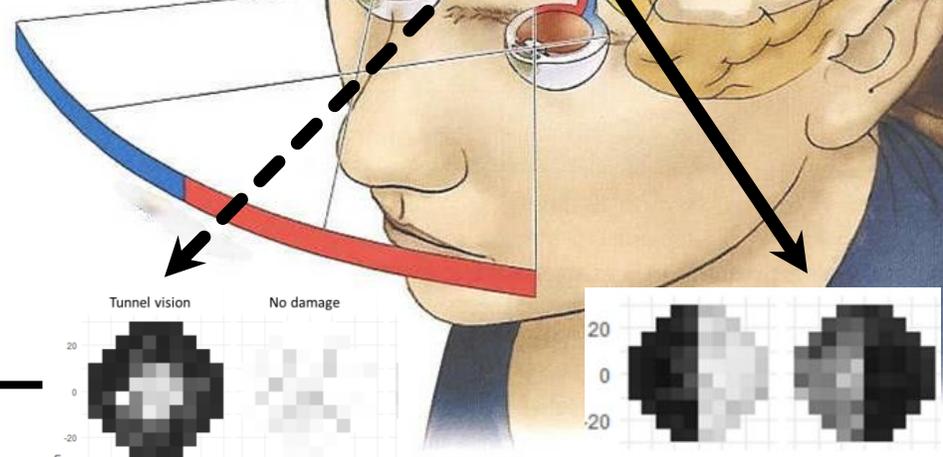
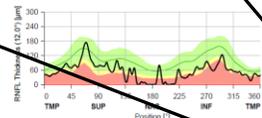
Function damage
(Electrophysiological signals)



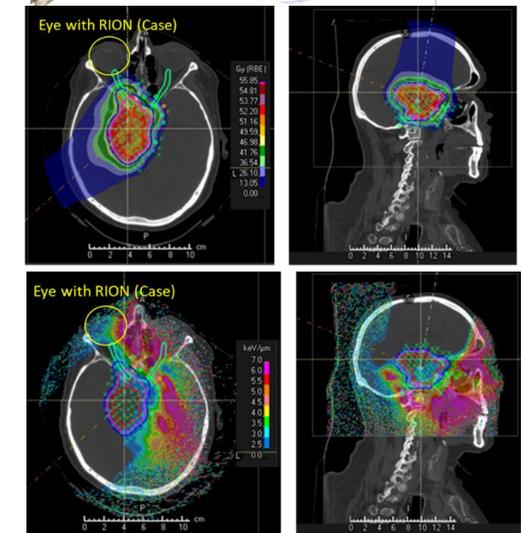
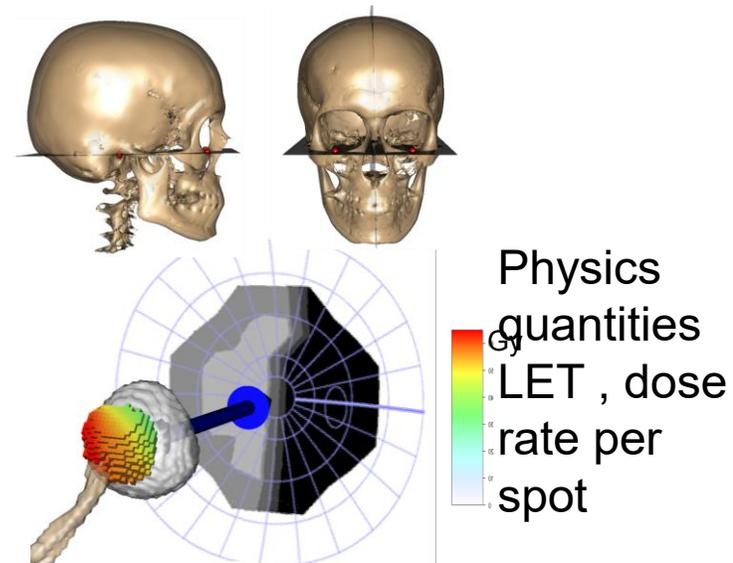
Structural damage



cataracte



5



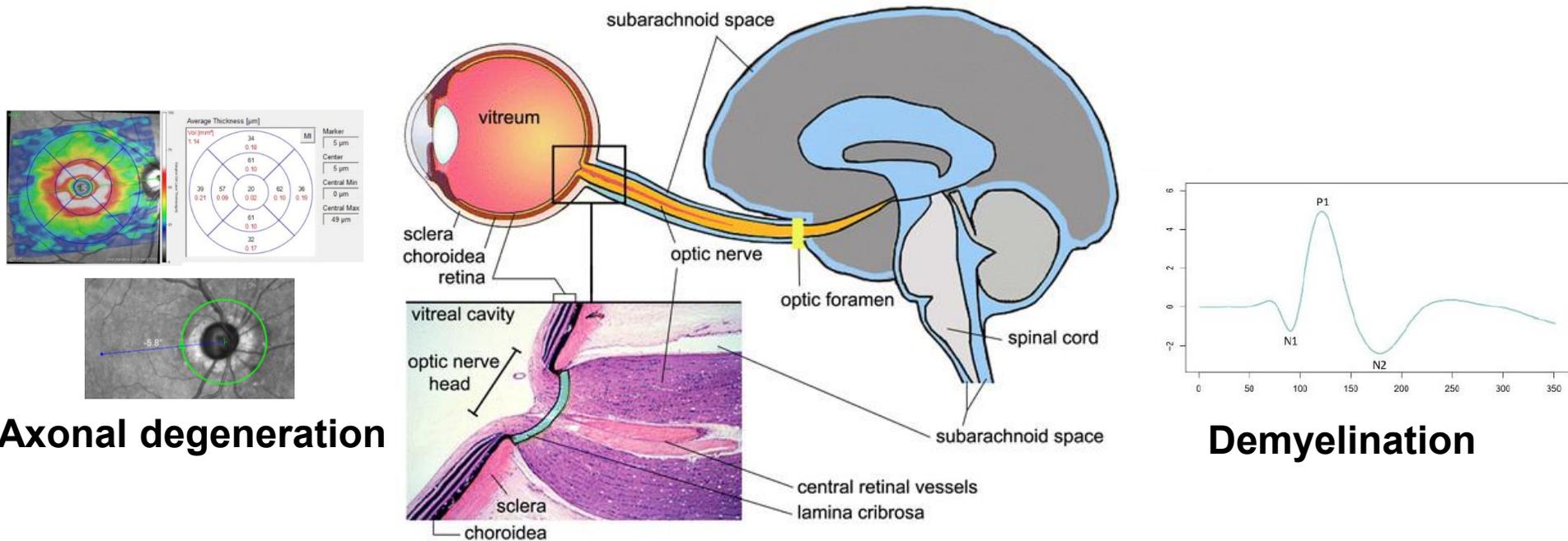
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A vertical column of logos on the left side of the slide. From top to bottom: CNRS (NUCLÉAIRE & PARTICULES), LPC CAEN, Centre Baclesse (unicancer NORMANDIE - CAEN), CYCLHAD (HADRON THERAPY FOR LIFE), NHa (NORMANDY HADRON THERAPY), and Université Caen Normandie.

Strategies to increase the level of evidence in France

Prospective multiscale cohorts

- Predictive and mechanistic modeling; actionable : **opportunity to define new treatments against toxicities**
- Exemple : optic neuropathy : vision loss





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Proton therapy

- Ongoing Trials
- On brain sparing and preservation of Cognitive function
- Collaborative 3-proton therapy center studies

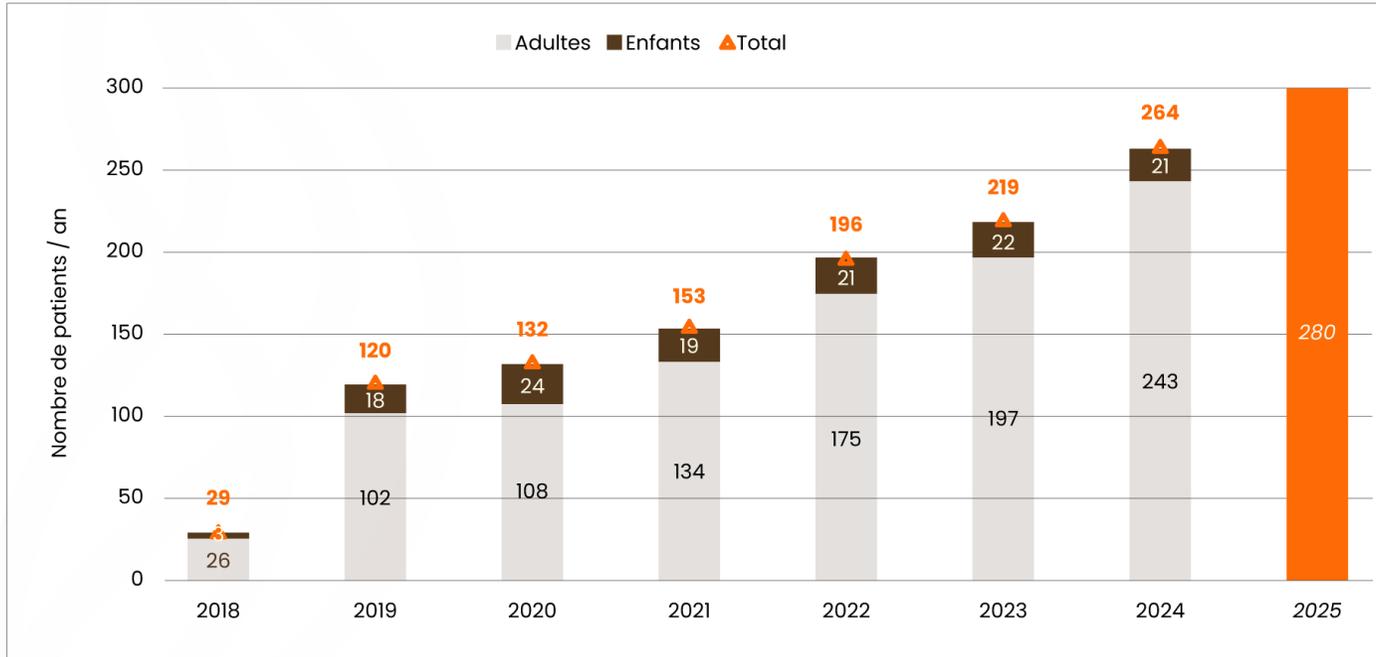


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Proton therapy ramp-up 2018-25 @Cyclhad-Centre Baclesse



Patients treated

Modern Proton therapy in France

> 2016 (IMPT / PBS + MFO)

+ Business plan compensated by the Region

Kids' referral (French registry): 1% in 2006 to 29% in 2021

30,000 fractions

1,300 patients

150 kids



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PROTON THERAPY IN CAEN : CYCLHAD FACILITY + CANCER CENTRE BACLESSE + NORMANDY HADRONTHERAPY



✓ Volume patients: TOP 1 Europe & TOP 3 Monde (1 salle ProteusONE)

✓ Note Google 4.9/5

✓ distractive methods for kids, Low grade Brain, Sinonasal, skin tumors

✓ 1 of the 20 multi-ions centres worldwide



✓ Unique centre for multi ion hadrontherapy in France

✓ 1st with a cyclotron

✓ Specific patient referral : sensitivity to uncertainties In field materials, robustness ...

Timely referral toward one of the 3 centres via PROTONSHARE platform or direct medical contacts ; Caen : protontherapie.caen@baclesse.unicancer.fr





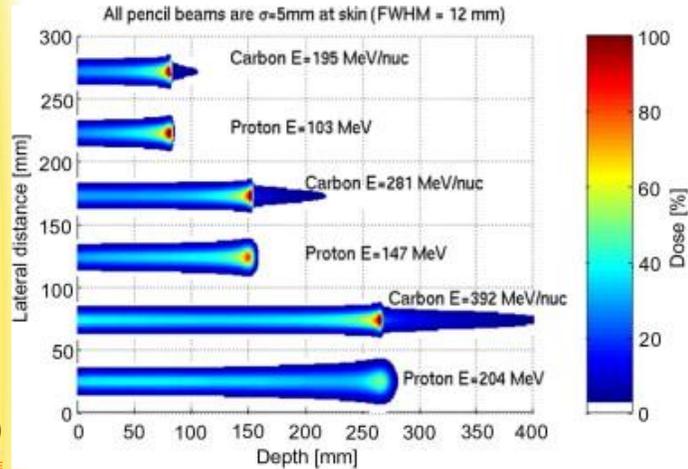
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Next challenges

Multi-ions hadrontherapy / C400 machine



		Ions			
		Proton	Helium	Carbon	Oxygene
Balistics	Distal penumbra	-	+	+/-	+/-
	Lateral penumbra	--	+	++	++
	Fragmentation tail	++	+/-	--	--
Biology	High TEL (ionisation density)	-	+/-	++	++
	RBE	+/-	+	++	++
	RBE Incertitude	+/-	+	++	++
	OER	--	--	+	++
Cost	Compared to proton	/	+/-	++	++

Courtesy of T Tessonier and JM Fontbonne

Implementation Timeline (Countdown)

- A project built at regional, national, and international levels
- A multi-ion prototype facility in France, in Caen
- Commercial proton therapy room S2C2
Clinical C400 room plus experimental radiobiology and physics rooms
- Application domains / clinical conditions / interdisciplinary collaboration
- Clinical C400 proton beam in 2026 (PTCOG so so) ?
carbon and helium beams planned for 2028 ?



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French ecosystem for multi ion hadrontherapy in Caen



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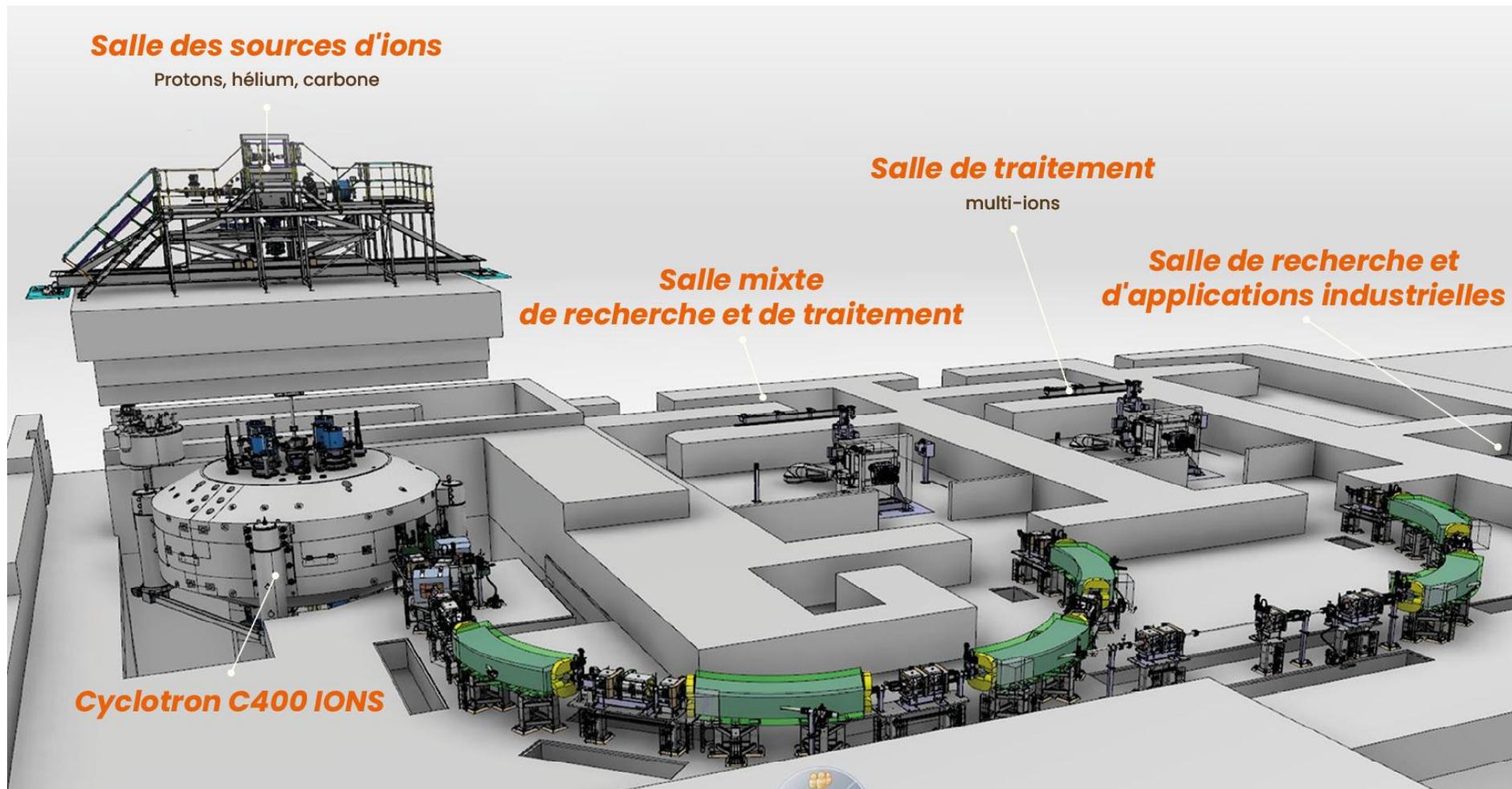


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C400 IONS

Vue aérienne



C400

Installation en cours – Premiers traitements en Carbone et Hélium à partir de 2028





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Indications of ions carbone

- Poor prognosis / radioresistant and inoperable tumors without a “magic bullet.” : Unmet need.
- **Carbon ions are not a better radiotherapy for everyone, but a better radiotherapy for some patients.**
- They are delivered using **hypofractionation**: typically 12–15 fractions (massive transition toward hypofractionation in France for all techniques)
- In some countries, such as Japan, indications extend further, including metastatic disease across many primary tumor types.



Clinical strategy

- **Treat each patient within a structured evaluation framework, from prospective cohort studies to randomized trials: evidence-based medicine to support reimbursement.**
- **Indications**
- **Conventional indications**
 - Re-irradiation
 - Large sarcomas
 - Melanomas
- **Innovative approaches**
 - Adaptive strategies (IGRT, ART)
 - Upright positioning (deformation modeling/AI, patient comfort, patient advocacy groups) versus supine positioning – dual approach
 - Immunotherapy combinations (radiation-induced lymphopenia mitigation, cold-to-hot immunogenic conversion) and targeted molecular therapies
- **Differentiating and disruptive techniques**
 - Personalized adaptive planning based on hypoxia
 - Carbon FLASH therapy – C400 specificity, early-phase development

Biological targeting

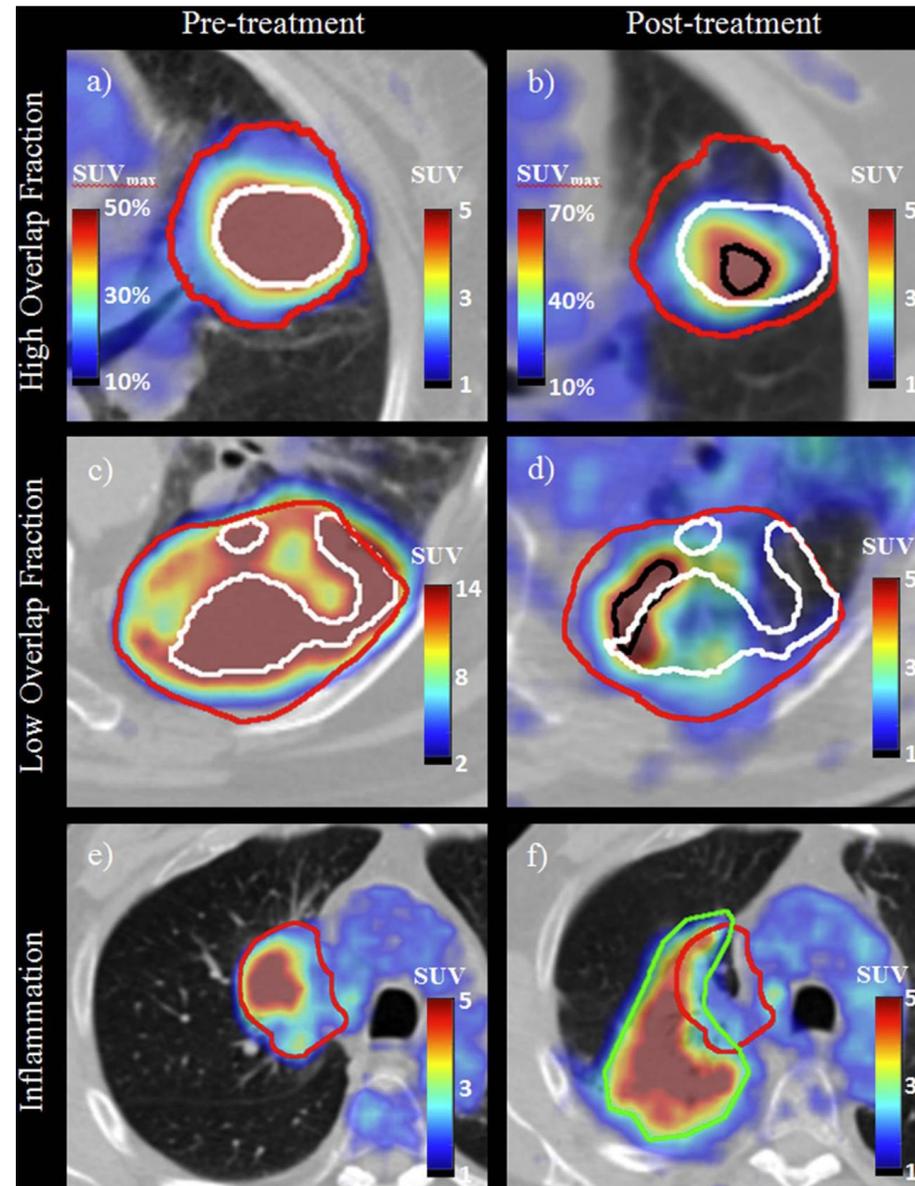
- Radiosensitive / hypoxic
- Challenges
- Tracers
- Dynamics of hypoxia over the course of RT
- Correlation with OER
- Dose prescription
- Fragmentation scale modeling
- Biological model

Relapse

Hypoxia?

relapse

Inflammation





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c400 positionnement patient mixte Upright + supine





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aRTwin: Virtually simulate each patient's trajectory across all treatment modalities before selecting and delivering the most appropriate radiotherapy strategy

Vivier de données pouvant être utilisées avec l'évolution des différents traitements cancéro

Algorithmes d'IA adaptés à chaque source de donnée pouvant évoluer avec l'état de l'art technologique

Chaque source de données clinique est représentée sous forme de **matrices**, un **graph** est par la suite construit sur ces matrices afin de représenter le patient.

Patient Physique

Pré traitement

Données cliniques
Images (IRM, scanner, ...)



Traitement (photon ou proton)

Planification
Dosimétrie



Post traitement

Données cliniques
Rapports de suivi (rechutes locales, globales, ...)



Collection et traitement des données automatisé

Nettoyage

Structuration

IA

Radiomiques SOTA : DINO v2-ViT

Données structurées (tabulaires) : Feature selection and engineering

Représentation numérique et algorithmes

Jumeau numérique

TEP

OAR

toxicités

Dosimétries

OAR

Similarité, comparaison et clustering en grande dimension
SOTA : Phénograph

Classification des toxicité / comparaison avec les modèles radiobiologiques NTCP

Application Web d'aide à la décision

Suggestion : Photon ou proton

Toxicité

Visualisations et comparaisons

Multiscale digital twins



Preclinical - One Health

- Veterinary medicine integrated with medical oncology and radiation oncology
- Preserving living resources: EU 4R-compliant; ethical and strategic approach
- Collaboration with Dallas and an expanded Normandy network (contact: Isabelle V., veterinary radiation oncologist)
- Treatment of dogs and cats:
- Oral melanomas, Large facial sarcomas, Gliomas
- (Indications suitable for carbon ions, protons, and helium ions)
- **Accelerating translation to human patients.**

Scientific committee

- Cyclhad and discussions with Baclesse, CNRS
- Designation of the strategic committee (3 already nominated)
- Sub groups / work packages being built
- First meeting March 9, 2026

- Equipments and modeling for the clinic
- Beam models (before those of the C400) installed in the TPS (RS fall-back / research dosimetry workstation)
- GATE beam line modeling (ongoing for S2C2 proton machine)

Scientific animation

- **SFNO Hadron4Life** (following on March 2025 symposium) monthly meetings, in English; to be extended to external attendees
- **Webinars** on proton therapy (Curie Dr Dendale, Caen Prof Thariat, Nice Prof Doyen) and carbon ions (Caen Prof Thariat, Luembourg Prof Vogin) planned in March, April 2026
- on behalf of the French Society of Radiation Oncology **SFRO**, which is very supportive ; current President Prof Olivier CHAPET
- With financial support from **CYLHAD**

SWOT ions carbonés en France



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+ Strengths

- Pic de Bragg
- Haut LET (carbone)
- Efficace même si hypoxie tumorale
- Dommages complexes faiblement réparables; Faible dépendance au cycle cellulaire; immunogénicité
- Dernier recours potentiellement curatif

↗ Opportunities

- Unmet needs (radio-résistance, ré-irradiation)
- Multi-ions
- Combinaisons innovantes

- Weaknesses

- Coûts
- Accès limité
- Biais d'adressage
- Bénéfice clinique variable
- Patients ayant une maladie de mauvais pronostic

⚠ Threats

- Preuves insuffisantes
- Queue de fragmentation
- Evaluer le risque M+ au traitement
- Pression médico-économique



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2026

WELCOME in CAEN / DEAUVILLE 8 - 12 June 2026

Track records for # of submitted abstracts

➤ 1600 attendees awaited

www.cyclhad.fr

CONSTITUTION DU COMITE SCIENTIFIQUE

PTCOG 64
DEAUVILLE 2026



64th ANNUAL PTCOG CONFERENCE

8 - 13 JUNE 2026
DEAUVILLE, NORMANDY
FRANCE



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French contributions



Clinique

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