Annual General Assembly

Delivering Affordable Proton Therapy Centre with Improved Medical Outcomes

25 July 2019

The following presentation of the AVO’s LIGHT® Proton Therapy Solution is part of our Development roadmap and is subject to conformity assessment(s) by AVO’s Notified Body as well as 510(k) clearance by the USA-FDA.
1 Introduction on Proton Therapy and Market Demand

2 Assessing the Sheer Size of a Proton Therapy Project – A Few Facts (from BBC)

3 Focus on the Harley Street Project

4 The Sites of Geneva and Daresbury – Selected Update

5 The Importance of FLASH

6 Conclusion and Q&A
Cancer will surpass cardiovascular diseases as #1 cause of death driven by population, ageing & lifestyle

More than 14,000 X-rays machines\(^1\) in the world are treating more than 60% of cancer cases

Radiotherapy is one of the most widely used and cost-effective treatment against cancer

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(1) Including cobalt-60 units (source: [https://dirac.iaea.org](https://dirac.iaea.org))


(3) OECD, % of patients treated. Source: BCG
Proton Therapy Provides Better Conformity and Sparing Healthy Tissue

Up to 60% less radiation to healthy tissue near the tumour, reducing damage and allowing for treatment near vital organs.

Increased possibility of re-treating cancers that have re-appeared or were not eliminated during first treatment.

Potential for larger dose of radiation that treats the tumour effectively, reducing the number of patient visits required.

Source: American Society of Clinical Oncology & BCG

Radiation (Gy): 31 29 28 24 15 9 2
Proton Therapy – Clear Acceleration Over the Past 10 Years

Total Patients Treated with Proton Therapy

Source: PTCOG, Proton Therapy World Market Report (MEDraysintel)
Need to Break the Current Status Quo

Only 81 centres today representing 209 treatment rooms

- Only c.62,700 patients can be treated worldwide based on current offering

Market currently growing at 12%+ per year...

- 125 treatment rooms ordered representing an additional treatment capacity of c.37,500 patients

... but more is needed to treat 2.9m patients at a minimum by 2040

- Implied number of treatment rooms to set up: more than 9,800 (3,300 centres)
- Implied CAGR 2018-2040: 19%

More than 9,000 additional treatment rooms needed by 2040!

(1) Source: PTCOG
(2) Assuming an average of 300 patients can be treated per annum per treatment room
(3) CAGR 2019-2023 based on orders booked as of that date
(4) Assuming 29.4m new cancer cases p.a. by 2040, of which 50% get radiotherapy; 20% of patients under radiotherapy receive proton therapy; based on an average number of 300 patients per annum per treatment room
(5) Net of the treatment rooms already in operations and ordered
(6) Assuming 3 treatment rooms per centre on average
## Topics

1. Introduction on Proton Therapy and Market Demand

2. **Assessing the Sheer Size of a Proton Therapy Project – A Few Facts (from BBC)**

3. Focus on the Harley Street Project

4. The Sites of Geneva and Daresbury – Selected Update

5. The Importance of FLASH

6. Conclusion and Q&A
80,000 m³ of Material Excavated
A Hole That Was 28m Deep...
... That Could Comfortably Fit the Royal Albert Hall
Concrete Maze to Absorb Radiation
Concrete Maze to Absorb Radiation – 4m Thick Walls (Cont’d)
128 Tonnes Door to the Concrete Maze
3,000 Lorry Loads of Concrete Delivered – 10 Olympic Pools Full of Concrete
Installation of a Cyclotron
90 Tonnes Cyclotron – More than a Fully Loaded Boeing 737
58 Tonnes Gantry and 300 Tonnes of Magnets; 83km of Cables
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Overview of the LIGHT System
All Items Transported in Standard Trucks

Modularity of LIGHT® Compared to Circular Accelerators

<table>
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<tr>
<th>Circular</th>
<th>LIGHT®</th>
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<td>1-2 large units</td>
<td>12 RF units</td>
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All Installation Activities through a Standard Bed Lift (2.7m High and 1.8m Wide)
No Absorbers Needed; Significantly Less Shielding Requirements

Shielding Walls, Accelerator Vault

150 cm Walls

Shielding walls vs competition: 40%
Reduced Footprint

Note: The indicative lay-out shows the entire UCLH site, of which the four floors below ground which will house the Proton therapy centre, including a 25 metres excavation. The five floors on top will house a haematological inpatient service and a short stay surgical centre.
The Harley Street Site – Accelerator Hall of only 156m²
The Harley Street Site – Accelerator Hall of only 156m²
Exposed concrete in the treatment spaces
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Geneva Offices and Test Facilities

- **P2 CERN Bunker** (at CERN French site) contains our LIGHT accelerator up to 52 MeV.
- **ATF2** (at CERN Meyrin site, 10 + 10 m²) for RF power units tests: Modulator+Klystron Systems (MKS).
- **FTF1** (outside CERN, near to our offices, 60 m²) for RFQ power IOT system developments and tests.
The Integration Site at Daresbury
8 Tonnes Transformer Delivered at Daresbury Laboratory
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A Focus on FLASH

Investigation on FLASH therapy using a high frequency linac for protons

A.M. Kokron1, A. Degiovanni2, J.B. Parr3

Background and rationale

FLASH is a technique that delivers high dose rates within 1-5 s (FLASH) to minimize tissue damage. This technique offers the possibility of higher treatment control, as with conventional radiotherapy (RT), and a potentially increased therapeutic ratio.

- Healthy tissue sparing allows for reduced toxicity with reduced normal tissue complications.
- The FLASH effect may depend on the presence of oxygen, which might change due to the patient's breathing or the treatment setup.
- The dose rate can be varied through a range of 1-5 s.
- Currently, various tracer and targeted agents are under investigation.

In this study, we investigated the potential of using proton pencil beam scanning (PBS) for uniform FLASH transients using a linear accelerator and compared the fractionation schedules.

Methods and Materials

A conventional treatment planning system (Kayser/Nichiatsu RTSS-60) was used. The treatment planning system (TPS) was used for dose calculations. The proton pencil beam simulator was used for dose calculations. The proton pencil beam simulator was used for dose calculations.

The study demonstrates that radiobiological dose calculations are an efficient tool for optimizing FLASH transients.

Acknowledgements

The authors acknowledge...

References


Figure 1: Graph showing dose rate vs. range for proton beam delivery. The dose rate increases as the range decreases.

Figure 2: Graph showing the dose rate vs. range for FLASH transients. The dose rate decreases as the range increases.

Figure 3: Graph showing the dose rate vs. range for uniform FLASH transients. The dose rate remains constant as the range increases.

Figure 4: Graph showing the dose rate vs. range for optimized FLASH transients. The dose rate increases as the range increases.
Current annual capacity for proton therapy (PT) = 62,700 patients

PT = 0.6/1.2% of radiotherapy

17-35x current PT capacity

PT = 20% of Radiotherapy

1.1-2.2m patients

With PT being priced competitively

2,700/5,400 additional PT rooms needed

At £15m per PT room

A demand for £41/81bn

PT = 75% of radiotherapy

4.1-8.1m patients

With FLASH

1 fraction per course (eg £5k/course)

10,200/20,400 additional PT rooms needed

At £15m per PT room

A demand for £152/305bn

60% more cancer cases by 2040

(29m new cases)

Assumptions

1. Based on WHO

2. % based on OECD data

3. Based on PTCOG, assuming 300 patients per room

4. Assuming 300/500 patients per year per room

5. Assumption: £15m per room

6. Assuming 900/1,500 patients per year per room

30/60% treated with radiotherapy

5.4/10.9m patients in 2018

18.1m cancer patients in 2018

(1)

(2)

(3)

(4)

(5)

(6)

30/60% treated with radiotherapy

5.4/10.9m patients in 2018

18.1m cancer patients in 2018

(1)

(2)

(3)

(4)

(5)

(6)
What is Next?

• **Proton source**
  • Manufactured
  • Delivered by end of September

• **RFQ**
  • Manufactured
  • Already delivered

• **4 SCDTLs**
  • Manufactured
  • Delivered by end of September

• **13 CCLs**
  • Manufactured
  • 6 already delivered and 7 to be delivered by early Q4:19

• **Treatment room hardware**
  • Manufactured
  • Delivered by end of December

• **First patient treatment**
  • By end of 2020
Building the Right Business Model

**TRANSACTIONAL**

**Customer:**
- State funding
- Cash milestone payment
- Full ownership of the system

**AVO:**
- Straight and simple sale

**HYBRID WITH REVENUE SHARE**

**Customer:**
- Limited pre-operation cash outlay

**AVO:**
- Partial cash sale of the system
- Possibility to leverage future upgrades of the system

**BUSINESS MODEL**

**LEASING**

**Customer:**
- No/limited pre-operation cash outlay

**AVO:**
- Secured lifetime rent
- Requires a dedicated leasing partner

**PPP**

**Customer:**
- No/limited pre-operation cash outlay

**AVO:**
- Lifetime revenue
- Possibility to leverage upgrades of the system
- Requires a dedicated financing vehicle

**Note:**
KOL: Key Opinion Leader
HCP: Healthcare Provider
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