Healthcare Equipment & Services

Source: Refinitiv

Market data

EPIC/TKR	**AVO**
Price (p)	**37.0**
12m High (p)	52.0
12m Low (p)	32.5
Shares (m)	237.6
Mkt Cap (£m)	87.9
EV (£m)	101.8
Free Float*	71%
Market	AIM

**As defined by AIM Rule 26*

Description

AVO is developing next-generation proton therapy systems for use in cancer radiotherapy. The first system is expected to undergo CE marking during 2020. Standard radiation procedures have evolved over many years. PBT delivers radiation via a beam of proton particles rather than a beam of photons used in conventional radiotherapy (X-rays).

Company information

Exec. Chairman	Michael Sinclair
CEO	Nicolas Serandour
	+44 203 617 8728
	www.avoplc.com

Shareholders

Liquid Harmony (Board)	18.9%
Other Board	9.9%
DNCA Investments	5.1%
P. Glatz	4.0%
Lombard Odier	3.3%
Brahma AG	3.3%
Barrymore Inv.	3.3%

Diary

4Q'19	All modules delivered
4Q'19	Patient positioning delivered

Analysts

Martin Hall	020 7194 7632
	mh@hardmanandco.com
Dorothea Hill	020 7194 7626
	dmh@hardmanandco.com
Grégoire Pavé	020 7194 7628
	gp@hardmanandco.com

ADVANCED ONCOTHERAPY

FLASH benefits from new US reimbursement

AVO's goal is to deliver an affordable and novel proton beam therapy (PBT) system, based on state-of-the-art technology developed originally at the world-renowned CERN. In the past 18 months, the project has been de-risked through important technical milestones. AVO is working on the verification and validation phase, prior to CE marking and LIGHT being used on the first patients. Proposed changes to the US reimbursement framework are beneficial to PBT as a whole, and the trend towards hypo-fractionation of ultra-high doses in a single patient visit (FLASH), for which LIGHT is uniquely positioned to deliver.

- **Strategy:** AVO is developing a compact and modular PBT system, which is affordable for the payor, financially attractive to the operator, and generating superior patient outcomes. AVO benefits from technology know-how developed by ADAM (CERN spin-off) and relies on a world-class supplier base.

- **US reimbursement:** The CMS is proposing to move from an unwieldy fee-for-service model to a radiation oncology model based on value of care for patients. This will encourage greater use of hypo-fractionation, which is beneficial for the PBT equipment providers who have a technology suited to hypo-fractionation and FLASH.

- **FLASH technology:** Oncologists are excited about the potential of FLASH technology, which can treat cancer patients in a single visit with potentially fewer side effects. Linear PBT systems have major advantages over conventional cyclotrons, leaving LIGHT uniquely positioned for FLASH.

- **Risks:** Since 2018, the more complex technical challenges have been overcome, and progress towards a fully-functional accelerator is under way in readiness for CE marking. Execution risk remains, but management's ability to raise funding and meet its milestones for the past 30 months has lowered this risk.

- **Investment summary:** AVO's market capitalisation of £102m equates only to the amount invested into LIGHT to date, which does not reflect either the enormous technical challenges that have been overcome, or the market potential. DCF analysis of the LIGHT prospects generates an NPV of at least 229p a share (fully-diluted). The disconnect between fundamental and market valuations offers an interesting investment opportunity.

Financial summary and valuation

Year-end Dec (£000)	2017	2018	2019E	2020E	2021E	2022E
Sales	0.0	0.0	0.0	21.5	65.5	111.5
Gross profit	0.0	-1.9	0.0	1.9	11.4	27.6
Administration costs	-12.9	-15.7	-15.0	-15.4	-15.8	-16.2
EBITDA	-14.1	-21.4	-18.9	-16.6	-10.5	1.6
Underlying EBIT	-14.5	-21.8	-20.6	-20.6	-14.6	-2.4
Statutory EBIT	-14.5	-21.8	-20.6	-21.2	-13.9	-0.7
Underlying PTP	-16.5	-21.9	-21.7	-22.3	-16.7	-4.6
Statutory PTP	-16.5	-21.9	-21.7	-22.9	-16.0	-2.9
Underlying EPS (p)	-17.6	-14.0	-8.9	-8.3	-6.1	-1.3
Statutory EPS (p)	-18.9	-13.4	-8.9	-8.5	-5.9	-0.7
Net (debt)/cash	-9.2	-2.0	-13.9	-21.5	-31.0	-34.7
EV/EBITDA	-	-	-	-	-	61.9

Source: Hardman & Co Life Sciences Research

Table of contents

LIGHT is nearing reality

Daresbury integration facility update

In May 2018, AVO signed a lease with the UK Government's Science and Technology Facilities Council (STFC) to establish a UK testing and assembly site in Daresbury (Cheshire). The first completed LIGHT machine will be assembled, verified, and validated on this site, prior to patient treatment.

At its 2019 AGM in July, management set out a schedule for the delivery of LIGHT components to Daresbury, which was updated in the 2019 interim results announcement in September.

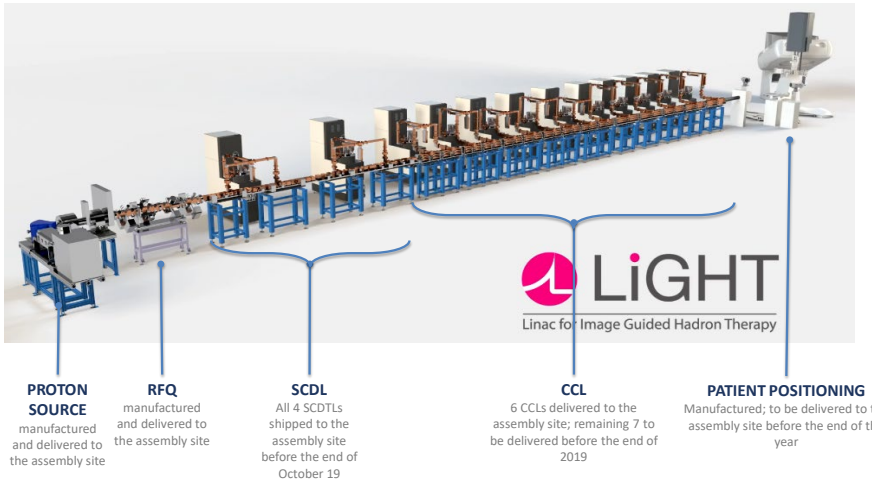
Delivery schedule for Daresbury

Component	#	Manufactured	As of 25 Jul 2019	As of 30 Sep 2019	Status
Proton source	1	✓	By end of September 2019	✓ Delivered	✓
RFQ	1	✓	✓ Delivered	-	✓
SCDTL	4	✓	By end of September 2019	✓ All delivered	✓
CCL	13	✓	6 delivered, 7 during 4Q'19	No change	In progress
Patient positioning	1	✓	By end of 2019	No change	In progress
On-site validation		N/A	Throughout 2019 and 2020	No change	In progress
First patient treatment		N/A	By end of 2020	No change	In progress

Source: Advanced Oncotherapy; Hardman & Co Life Sciences Research

The key modules and components that comprise LIGHT have all been manufactured, and most have been delivered to Daresbury. The remaining seven CCLs and the patient positioning system are expected to be delivered on site during 4Q'19. Each step of this process means that AVO is entering a less risky, less cash-intensive phase of verification and validation in readiness for CE marking.

Getting LIGHT ready for the verification and validation phase



Source: Company announcements

What's next?

The next stage of AVO's execution plan focuses largely on the verification and validation process.

Verification and validation processes are used for checking that a product meets requirements and specifications and that it fulfils its intended purpose. These are critical steps of a quality management system, such as ISO 13485, which the company obtained in January 2019.

- **Verification** is intended to check that LIGHT meets a set of design specifications. In the development phase, verification procedures involve performing special tests to model or simulate a portion, or the entirety, of the LIGHT system, then performing a review or analysis of the modelling results. In the post-development phase, verification procedures involve regularly repeating tests devised specifically to ensure that LIGHT continues to meet the initial design requirements, specifications, and regulations as time progresses. Verification can be in development, scale-up, or production. This is often an internal process.
- **Validation** is intended to ensure that the LIGHT system meets the operational needs of the user. It is a process that provides a high degree of assurance that LIGHT accomplishes its intended requirements.

The verification and validation phase allows for completion of the documentation required for the CE marking and, as such, is an important step forward, prior to LIGHT being used on the first patients.

Recent developments in PBT

Background information

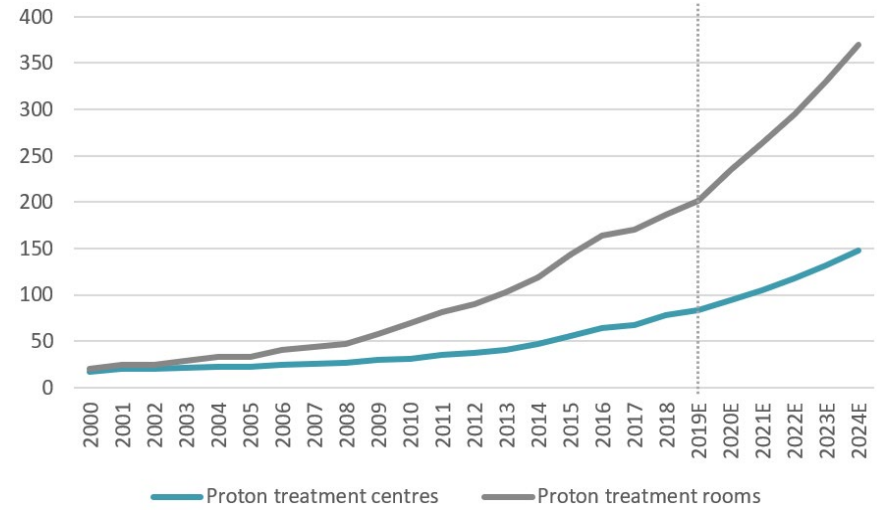
PBT is a medical technology that has seen significant development and a wider adoption in the past few years

Standard radiation procedures have evolved over many years. Proton beam therapy (PBT) delivers radiation via a beam of proton particles rather than X-rays making it an alternative to conventional radiotherapy. The physical properties of protons result in a significantly reduced dose of radiation being deposited in normal tissue before and beyond the tumour. This is due to the "Bragg-Peak" effect, a physical phenomenon, that concentrates the killing energy of protons onto the tumour, allowing greater precision and higher doses compared with X-rays, while minimising the damaging effect on surrounding tissue.

PTCOG estimates that there are 84 specialist treatment centres globally, operating 201 treatment rooms

Technical upgrades to proton therapy systems – most notably the development of the pencil-beam feature, which reduces the "scattering effect" and pinpoints precisely the proton beam on the tumour, coupled with cost reductions – have led to a fast acceleration in the number of machines/systems sold, particularly over the past 15 years. According to Particle Therapy Co-Operative Group[1] (PTCOG), from 2009 to 2018, there was a sharp uptake in the number of proton treatment centres, with a CAGR of 12%. Currently, PTCOG estimates that there are 84 specialist centres with 201 treatment rooms in operation worldwide. With around 2.5 rooms per proton centre, mainly driven by the Chinese market, we can conservatively estimate a total of 148 proton centres and 370 treatment rooms by 2024.

Installed base of proton treatment centres and rooms – 2000 to 2024



E: Hardman estimate
Source: PTCOG

Currently, PBT is mainly used for childhood cancers and tumours that develop in the head and neck or close to the spinal column and in other sensitive organs.

An NHS policy document on PBT underscores its benefit:

> *"One third of survivors of childhood cancer report severe or life-threatening complications up to 30 years after the diagnosis of cancer. This can be due to side effects of cancer treatment and radiotherapy is a significant contributing factor."*

Source: NHS England Clinical Commissioning Policy

[1] https://www.ptcog.ch/

PBT is particularly effective in treating children and teenagers where any residual damage from radiotherapy could lead to developmental delays, hormonal deficiencies, and issues with bone and muscle growth.

Treatment of head and neck carcinomas requires high doses of radiotherapy to sensitive areas such as the front of the brain, base of the skull, mouth and facial bones. Research has demonstrated that patients experience less exposure to radiation with PBT compared with standard radiotherapy. Tumours that develop close to the spinal cord are difficult to reach, but PBT is extending clinicians' ability to treat these accurately, reducing the jeopardy of secondary tissue damage.

A potential to be unlocked with the development of more cost-effective and medically superior PBT systems

As highlighted in a previous report[2] on the company *Commercialising a breakthrough technology*, dated 13 May 2019, the market is desperately looking for new proton therapy systems that can reduce the initial capital expenditure, including the building and installation costs, as well as the operating costs of the hospitals and, by implication, the treatment cost per patient. This is expected to result in a wider market adoption and the use of PBT across a larger range of indications. In our opinion, the ability to reduce the treatment cost at a level closer to conventional radiotherapy will help to unlock the potential of proton therapy and its use for a wider range of indications.

New developments

There have been two notable industry developments during the past few weeks, which bode very well for the continuing development and wider adoption of PBT in general and, in our opinion, for AVO in particular:

- evolution of the reimbursement environment, particularly in the US; and
- recognition and enthusiasm for the benefits of FLASH technology.

The relevance of these developments is discussed in the following two sections.

[2] Hardman & Co Life Sciences research report – 13 May 2019

More favourable reimbursement

Background

With healthcare costs continuing to rise globally, reimbursement policies adapt continuously. In the US, the largest healthcare market, reimbursement is currently based on an unwieldy fee-for-service model where services are unbundled and paid for separately. This has resulted in a fragmentation of care, with no single group taking responsibility for the health of the patient or the cost of services rendered. In addition, gaps in communication between care providers have resulted in repeat services and excessive costs. In response, the Centers for Medicare & Medicaid Services (CMS) announced that it intends to launch a radiation oncology model that would make prospective payments to cover radiotherapy services, in 90-day episodes, for patients diagnosed with 17 types of cancer. This proposal is expected to start next year and run until 2024.

Current CMS approach

- Radiation oncologists provide time-limited specialty services for cancer patients – usually do not manage all of a patient's care needs.
- Multiple forms of radiation therapy – Electron Beam (multiple versions), Brachytherapy, Proton Beam Therapy, Neutron Beam Therapy.
- Services are primarily provided in free-standing radiation therapy centres (physician offices) and Hospital Outpatient Departments (HOPDs).
- Services are expensive – Medicare spent more than $7.2bn on radiation therapy episodes 2013-15, or roughly $2.4bn p.a.

Rationale for change

- Address site of service payment differentials – i.e. higher payment rates in HOPDs vs. community settings for the same service.
- Address coding and payment challenges, creating less volatility in revenue year-on-year.
- Empower patients and doctors by encouraging physicians to provide high-quality nationally recognised evidence-based care.
- Support innovative approaches to improving quality, accessibility, and affordability by removing current payment incentives.
- Opportunity for radiation oncologists to provide the most appropriate care for their patients without negative financial consequences.
- Improve beneficiary experience by rewarding high-quality patient-centred care and providing incentive for high-value radiotherapy.

Proposed model

- Prospective, site neutral episode payment for radiation therapy services; with annual retrospective payment reconciliation.
- 90-day episodes for radiation therapy services for 17 cancer types.
- Bundled payments would be:
  - Nationally based
  - Adjusted for participant experience and case mix
  - Triggered by provision of treatment planning service
  - Modality agnostic – specifically includes PBT
  - Split into professional and technical services

- Required participation in randomly selected Core-Based Statistical Area (CBSAs); 40% of all eligible radiotherapy episodes will be included in the model.
- Participants furnish professional RT services, technical RT services, or both. Participants to include physician group practices including specialist centres, and HOPDs.

Proposed model design – course of treatment and included services

Consultation	Treatment planning	Technical preparation & special services
Initial consultation typically billed using E&M service **Excluded**	Determine treatment modality, parts of the body that must be irradiated, and plan for radiation treatment *Excludes:* Radiation therapy planning	Technical preparation to ensure radiation dosing is accurate, machine is prepared, treatment aids are constructed *Excludes:* Radiation treatment aids
Treatment delivery	**Treatment management**	**Other exclusions**
Radiation delivered to patient in one or more sessions *Excludes:* Radiation treatment delivery, and apply intracavity radiation brachytherapy	Patient monitoring, treatment adjusted according to outcomes *Excludes:* Radiation treatment management x5 treatments	Experimental and low volume treatments (neutron beam, hyperthermia) Surgical services supporting brachytherapy General imaging not related to radiation preparation Radiation therapy outside hospital or specialist radiation centre settings

Source: Adapted from Centers for Medicare & Medicaid Services

Implications for PBT

Shift towards value-based care model represents a compelling opportunity for companies such as AVO

This change in the US reimbursement policy has direct implications on proton therapy, as a sub-segment of the broader radiation market. Currently, the total dose of radiation delivered to patients is divided into several, smaller doses (also called fractions) over a period of several weeks. This maximises the effect of radiation on cancer and minimises the negative side effects. The CMS proposal signals a trend whereby reimbursement is based on value of care and hence encourages the greater use of hypo-fractionation (i.e. fewer patient visits to hospital). This announcement is great news for the proton therapy equipment providers that offer systems which can facilitate hypo-fractionation of radiotherapy. In that regard, AVO is in a unique position (see next section).

Timetable

Pending publication of the final rule, these changes are expected to be implemented between January and April 2020.

Timetable for introduction

Date	Event
18 Jul 2019	Notice of proposed rulemaking (NPRM)
16 Sep 2019	Public comment period ends
4Q'19	Final rule published (pending)
4Q'19	Participants receive their specific payment amounts (pending final rule publication)
1Q'20	Model Launch (pending final rule publication)

Source: Adapted from Centers for Medicare & Medicaid Services

Rising interest in FLASH

Background

FLASH – the opportunity to shift the treatment paradigm in radiation therapy

Radiotherapy is a core modality for cancer treatment, with nearly 50% of patients undergoing radiotherapy as part of their treatment (CRUK). The goal of radiation therapists and new technologies has been focused on finding the optimal balance between damaging cancerous cells and preserving normal tissue from the harmful effects of ionising radiation. To date, the best methods of achieving this have been dose fractionation (i.e. dividing the high dose of radiation into a course of therapy over many visits) and precise volume optimisation (i.e. high precision radiotherapy to ensure that the targeted tissue volume is receiving the high dose of radiation and to allow for movements of target and normal tissue).

Ultra-fast delivery of very high doses of radiation

While both these methods have improved patient outcomes, oncologists are extremely excited about a third method, called FLASH radiotherapy. This relies on the ultra-fast delivery (i.e. pulses of less than a second) of the radiation treatment at dose rates that are orders of magnitude greater than those currently in routine clinical practice (i.e. 40 to 120 Gy vs. 2 Gy per treatment).

Benefits of FLASH

Potential to reduce patient visits from up to 35 down to 1-3

FLASH represents the ideal scenario for hypo-fractionation since the number of fractions is limited potentially to one or three fractions or patient visits depending on the tumour size, giving enormous patient benefits compared with conventional courses of treatment, which usually involve up to 35 fractions over many visits.

In addition, this has a clear financial impact for the operator given the shift towards value-based care and reimbursement for the entire treatment course as described in the previous section, as opposed to a reimbursement per fraction currently used.

FLASH, therefore, is an exciting opportunity, with proton therapy being a particularly promising modality to achieve the desired outcomes. While this new therapy is currently in the pre-clinical testing phase, animal data to date and first patient outcomes bode very well for the future.

Scientific publications on FLASH

Growing interest in FLASH

Recent reports – in particular from the recent AAPM[3] meeting in San Antonio – support the delivery of ultra-high doses of radiation and the fact that it can accurately target tumours with vastly reduced toxicity of normal tissue. On that note, Dr Pollard-Larkin from MD Anderson Cancer Center gave a talk entitled: "*FLASH photon: one small step for physics, one huge leap for cancer therapy*". As highlighted below, there has been a significant increase of scientific publications featuring FLASH as an opportunity to optimise patient care.

FLASH publications – 2014 to present

38 ***FLASH/FLASH related publications by midyear 2019***

Source: Varian 2019 PTCOG presentation

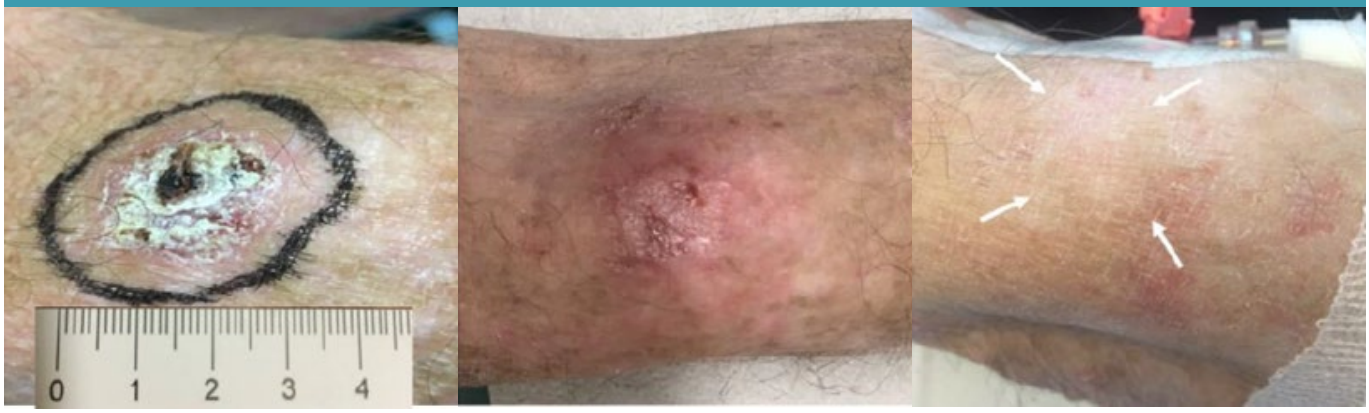
[3] American Association of Physicists in Medicine

First patient treatment

Outcomes from the first case report of FLASH radiotherapy in a human patient was published in October[4]: a 75-year-old man who had previously undergone 110 localised radiotherapy courses over the past decade for different lesions. Although his tumour control has been good, treatment was associated with severe skin toxicity. His latest cutaneous T-cell lymphoma was treated using FLASH at Lausanne University Hospital.

In this single-patient study, a 3.5cm ulcerated lesion was treated via a prototype Oriatron 5.6MeV linear accelerator (linac) specifically engineered for accelerating proton in a FLASH mode and to deliver 10 pulses of radiation, totalling 15 Gy, in 90 ms. Of note, the patient felt no sensation during treatment.

Evolution of lesion



Day 0 | 3 weeks | 5 months

Source: Adapted from Bourhis et al.[4]

The pictures show the evolution of the cutaneous lymphoma from immediately prior to FLASH treatment, through the response at three weeks to complete healing at five months. The only side effect was the grade 1 epithelitis (reddening of the skin) and oedema in the tissue surrounding the skin at three weeks. The authors concluded that the tumour response was rapid, complete and durable and that there was limited effect on the surrounding normal skin, and FLASH radiotherapy was feasible, safe and deserved further clinical evaluation.

LIGHT ideally suited for FLASH

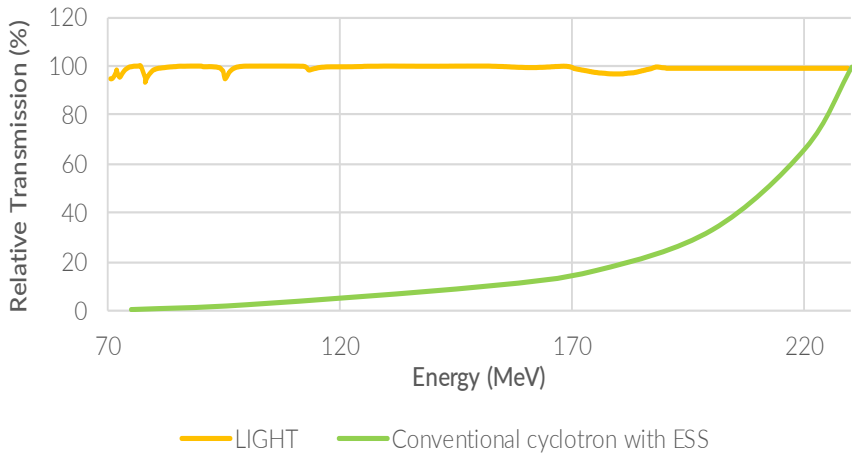
As highlighted above, the energy level directly correlates to the depth at which the radiation is deposited (the Bragg peak effect). Cyclotrons are circular proton accelerators, which generate higher energy levels of protons than required and then use degraders and range shifters for the purpose of reducing the energy to the level required for treatment. A consequence of using these degraders/range shifters is that a large proportion of protons are disseminated in the accelerator hall, creating unwanted radiation that requires large concrete shielding walls, usually in excess of six metres thick. This issue is further compounded by the fact that FLASH requires significantly more protons per fraction (i.e. a dose of 60Gy vs. 2Gy per fraction), exacerbating this situation, and making the use of FLASH an unrealistic goal due to the need to have even greater shielding. In addition, customisation of existing cyclotrons and facilities would require considerable operational down-time, which would be counter-productive to the current demand for PBT, and would not make commercial sense for the operator.

[4] *Bourhis et al., 2019*

LIGHT is ideally suited for FLASH and hypo-fractionation

In contrast, AVO's LIGHT system is particularly well suited for being the future treatment of choice for FLASH. Being linear, the system generates an electronically controlled proton beam of the required energy level. This electronic control of the beam removes the need for absorbers, and hence makes LIGHT ideally suited for FLASH at ALL energies and for any radio-sensitive tumours independently on their depths.

Transmission vs. maximum output (%)



Source: Company website

Competitive landscape

Unsurprisingly, given all the excitement surrounding the potential of FLASH radiotherapy to generate hypo-fractionation of ultra-high doses to improve patient outcomes, all the current manufacturers are investigating how their existing cyclotron-based systems can be adapted/customised to provide this technology. A summary of the current position of competitors with respect to FLASH technology is provided in the appendix (see page 19).

Conclusion

In the case of LIGHT, the promise of FLASH represents a golden opportunity, as it would be the only high energy linac-based PBT available on the market. Data presented by AVO scientists at the recent PTCOG meeting in Manchester[5] support the use of FLASH for all indicated tumours, regardless of their depth within the body. Results from the study "*Investigation on FLASH therapy using a high frequency linac for protons*" were presented. The scientific community appreciated the versatility of LIGHT, which was featured in the keynote speech.

[5] 58th Annual Conference of the Particle Therapy Co-Operative Group (PTCOG58), Manchester, England, 10-15 June 2019

Financing update

Capital increase

Since the beginning of the year, AVO has raised ca.£40.8m of financing through a combination of equity (ca.£26.5m) and debt (£14.0m). 70% of the new equity raised has been done with the support of new investors, which highlights that the shareholder base is becoming more diversified.

Funding during 2019

Date	Equity (£m)	Debt (£m)	Comment
January 2019	10.0	-	Subscription at 40p per share
May 2019	2.4	10.0	Subscription at 40p per share
August/September 2019	14.4	4.0	Same terms; includes conversion of prev. loan
	26.8	**14.0**	

Source: Company announcements

- Equity was issued at 40p per share to new and existing shareholders.
- The £10m loan is with Credit Suisse, at 2%+LIBOR per annum and is repayable in full in cash at the end of the 24-month period.
- The unsecured loan of £4.0m is with Nerano Pharma, carries a coupon of 12% p.a., and has a term of five years.

IFRS 16, consequences for AVO financials

From 1 January 2019, the new international accounting standard IFRS 16 became effective and requires companies to report leases, measured at the present value of the lease payments, on the balance sheet. This has the effect of boosting fixed assets, but also increasing financial liabilities, affecting the net cash position. Prior to IFRS 16, these liabilities were off-balance sheet. There is no requirement for companies to re-state previous financial periods.

The lease liability associated with Daresbury was included in AVO's interim statement. The company currently has lease liabilities of £9.3m. This was countered by an increase in fixed assets from £4.1m to £15.3m. These figures are expected to increase further to reflect the addition of the lease liability associated with the Harley Street site.

Influence of IFRS 16 on AVO

Year-end Dec	2018		2019	
(£m)	Actual	1H'19 actual	*Previous FY forecast	New FY forecast
Fixed assets	4.09	15.26	4.1	16.1
Invested capital	52.48	71.19	57.9	72.5
Long-term leases	n/a	-7.94	n/a	-7.3
Short-term leases	n/a	-1.33	n/a	-1.3
Long-term loans	0.00	-9.35	-14.0	-14.0
Short-term debt	3.00	-2.23	-0.0	-0.0
Cash	1.01	3.59	12.9	8.7
Net cash (debt)	**-1.99**	**-17.26**	**-9.0**	**-13.9**

**Prior to August/September capital increase and adoption of IFRS 16*
Source: Hardman & Co Life Sciences Research

Financial forecasts

Apart from the introduction of IFRS 16 and increased interest costs, there have not been any material changes to forecasts since out latest publication.

Profit & Loss

- **Administration costs:** Reported administrative costs represent a combination of administration costs (general corporate overhead), marketing spend (directly related to LIGHT), and share-based costs.
- **General overhead:** Despite some anticipated personnel appointments, general administration is forecast to remain reasonably stable over the coming years.
- **Marketing and R&D spend:** As LIGHT nears completion, there will be an inevitable marketing spend to support system sales. Also, further refinements, e.g. use of FLASH technology, will result in some future R&D investment.
- **Profitability:** Based on our LIGHT forecasts (see research dated 13 May 2019[2]), AVO will become profitable at both the EBITDA and EBIT levels in fiscal 2022.

Profit & Loss account						
Year-end Dec (£m)	**2017**	**2018**	**2019E**	**2020E**	**2021E**	**2022E**
LIGHT systems sold	0	0	1	1	2	3
Cumulative systems	0	0	0	2	4	7
Cumulative rooms	0	0	0	1	4	10
Sales	0.0	0.0	0.0	21.5	65.5	111.5
COGS	0.0	-1.9	0.0	-19.6	-54.0	-83.8
Gross profit	0.0	-1.9	0.0	1.9	11.4	27.6
Marketing costs	0.0	0.0	-1.0	-1.1	-3.1	-5.2
Administration costs	-12.9	-15.7	-15.0	-15.4	-15.8	-16.2
Share-based costs	-1.5	-4.2	-4.6	-5.0	-5.5	-6.3
R&D (future development)	0.0	0.0	0.0	-1.1	-1.6	-2.4
Other income	0.0	0.0	0.0	0.0	0.0	0.0
Underlying EBITDA	**-14.1**	**-21.4**	**-18.9**	**-16.6**	**-10.5**	**1.6**
Depreciation	-0.4	-0.4	-1.7	-1.7	-1.8	-1.8
Amortisation	0.0	0.0	0.0	-2.3	-2.3	-2.2
Underlying EBIT	**-14.5**	**-21.8**	**-20.6**	**-20.6**	**-14.6**	**-2.4**
Share of JV profit/(loss)	0.0	0.0	0.0	-0.6	0.7	1.7
Exceptional items	0.0	0.0	0.0	0.0	0.0	0.0
Statutory EBIT	-14.5	-21.8	-20.6	-21.2	-13.9	-0.7
Net interest	-2.0	-0.1	-1.2	-1.7	-2.2	-2.2
Underlying PBT	**-16.5**	**-21.9**	**-21.7**	**-22.3**	**-16.7**	**-4.6**
Other financials	0.0	0.0	0.0	0.0	0.0	0.0
Extraordinary items	0.0	0.0	0.0	0.0	0.0	0.0
Statutory PBT	-16.5	-21.9	-21.7	-22.9	-16.0	-2.9
Tax payable/credit	2.8	0.8	3.3	2.0	1.0	1.2
Underlying net income	**-13.7**	**-21.1**	**-18.4**	**-20.3**	**-15.7**	**-3.4**
Forex gain/loss	-1.1	1.0	0.0	0.0	0.0	0.0
Statutory net income	-14.7	-20.2	-18.4	-20.9	-15.0	-1.7
Ordinary 25p shares:						
Period-end (m)	72.5	169.6	237.6	253.0	260.0	267.0
Weighted average (m)	77.8	150.5	207.1	245.3	256.5	263.5
Fully-diluted (m)	91.4	188.2	249.2	280.4	284.6	284.6
Underlying basic EPS (p)	**-17.6**	**-14.0**	**-8.9**	**-8.3**	**-6.1**	**-1.3**
Statutory basic EPS (p)	-18.9	-13.4	-8.9	-8.5	-5.9	-0.7
Underlying fully-diluted EPS (p)	-14.9	-11.2	-7.4	-7.2	-5.5	-1.2
Statutory fully-diluted EPS (p)	-16.1	-10.7	-7.4	-7.4	-5.3	-0.6
DPS (p)	0.0	0.0	0.0	0.0	0.0	0.0

Source: Hardman & Co Life Sciences Research

Balance sheet

- **Net cash/(debt):** Introduction of IFRS 16 regarding lease liabilities has affected the net cash/(debt) calculation. At the interim stage, net debt was -£17.3m, comprising gross cash of £3.6m and financial liabilities of -£20.9m.
- **Capital increase:** In August/September 2019, the company raised a gross new capital of £18.4m, made up of a £14.4m equity issue (gross, including loan conversion) and a new loan of £4.0m.
- **Fixed assets:** Implementation of IFRS 16 has also been reflected in the increased recognition of fixed assets, which stood at £15.3m at 30 June 2019, compared with £4.1m at 31 December 2018.
- **Working capital:** There will inevitably be a build-up in debtors and creditors, as the company signs contracts for LIGHT systems and places orders with its manufacturing partners for the various modules.
- **1H'19 results:** Depreciation charges, capital expenditure and capitalised R&D were all higher than anticipated, which has had a knock-on effect on our 2019 full-year forecasts. These items, coupled with the introduction of IFRS 16, account for the change in our net cash/(debt) calculation.

Balance sheet						
@31 Dec (£m)	2017	2018	2019E	2020E	2021E	2022E
Shareholders' funds	28.7	34.0	42.1	31.2	16.2	14.4
Cumulated goodwill	0.0	0.0	0.0	0.0	0.0	0.0
Total equity	28.7	34.0	42.1	31.2	16.2	14.4
Share capital	20.2	42.4	59.4	63.2	65.0	66.7
Reserves	8.4	-8.4	-17.3	-32.1	-48.8	-52.3
Provisions/liabilities	0.0	16.5	16.5	16.5	16.5	16.5
Lease liabilities	0.0	0.0	8.6	7.3	5.9	4.6
Long-term loans	0.0	0.0	14.0	24.0	24.0	24.0
Short-term debt	9.2	3.0	0.0	0.0	0.0	0.0
less: Cash	0.1	1.0	8.7	9.8	-1.0	-6.1
Invested capital	**37.9**	**52.5**	**72.5**	**69.2**	**63.6**	**65.7**
Fixed assets	1.2	4.1	16.1	14.8	13.6	12.4
Intangible assets	30.6	40.2	46.2	45.9	44.6	42.3
Investments	0.3	0.3	0.3	0.3	0.3	0.3
JV investment	0.0	0.0	0.0	3.0	3.0	3.0
Inventories	7.6	10.0	13.5	17.0	17.5	25.4
Trade debtors	*0.0*	*0.0*	*1.5*	*2.1*	*6.3*	*10.3*
Other debtors	*2.8*	*3.2*	*3.2*	*3.2*	*3.2*	*3.2*
Tax liability/credit	*2.9*	*0.7*	*3.3*	*2.0*	*1.0*	*1.2*
Trade creditors	*-4.0*	*-2.8*	*-1.9*	*-2.0*	*-2.1*	*-2.2*
Other creditors	*-3.5*	*-3.2*	*-9.6*	*-17.1*	*-23.8*	*-30.3*
Debtors less creditors	-1.8	-2.1	-3.6	-11.8	-15.4	-17.8
Invested capital	**37.9**	**52.5**	**72.5**	**69.2**	**63.6**	**65.7**
Net cash/(debt)	**-9.2**	**-2.0**	**-13.9**	**-21.5**	**-31.0**	**-34.7**

Source: Hardman & Co Life Sciences Research

Cashflow

- **Working capital:** The strategy to facilitate vendor financing arrangements with purchasers is aimed at securing working capital. However, there will still be a working capital requirement during the ramp-up phase.
- **Harley Street:** As part of the JV arrangement with Circle Health, AVO is committed to an investment of £3.0m in fiscal 2020.
- **Capitalised spend:** The high intangible expenditure of £8.8m in 2018 included, in part, investment at the Daresbury site, which is expected to reduce significantly from 2019.
- **Loans/capital increases:** To date in 2019, AVO has raised a total of £40.8m new capital through a mixture of equity (£26.8m gross) and loan facilities (£14.0m). An assumption has been made that future loans will be taken against contracted orders for LIGHT.
- **Warrants:** At the end of 2018, AVO had 34.5m warrants outstanding, which are exercisable over the coming years, with the potential to raise ca.£8.0m of new capital. This is reflected over the forecast period.
- **Cashflow breakeven:** Based on our central-case LIGHT forecasts, we believe that AVO will reach operational cashflow breakeven at the end of fiscal 2023.

Cashflow						
Year-end Dec (£m)	2017	2018	2019E	2020E	2021E	2022E
Underlying EBIT	-14.5	-21.8	-20.6	-20.6	-14.6	-2.4
Depreciation	0.4	0.4	1.7	1.7	1.8	1.8
Amortisation	0.0	0.0	0.0	2.3	2.3	2.2
Share-based payments	1.5	4.2	4.6	5.0	5.5	6.3
Inventories	*-0.2*	*-4.3*	*-3.5*	*-3.5*	*-0.5*	*-7.9*
Receivables	*-2.1*	*0.0*	*-1.5*	*-0.6*	*-4.2*	*-4.0*
Payables	*4.3*	*-1.4*	*-0.9*	*0.1*	*0.1*	*0.1*
Change in working capital	2.0	-5.7	-5.9	-4.0	-4.6	-11.8
Exceptionals/provisions	-0.8	18.0	0.0	0.0	0.0	0.0
Other	0.0	0.8	0.0	0.0	0.0	0.0
Company op. cashflow	**-11.4**	**-4.0**	**-20.2**	**-15.6**	**-9.6**	**-3.8**
Net interest	-0.6	-0.1	-1.2	-1.7	-2.2	-2.2
Lease payments	0.0	0.0	-0.7	-1.3	-1.3	-1.3
Tax paid/received	3.1	2.9	0.7	3.3	2.0	1.0
Operational cashflow	**-8.9**	**-1.2**	**-21.3**	**-15.3**	**-11.1**	**-6.4**
Capital expenditure	-0.1	-3.3	-2.5	-0.5	-0.6	-0.6
Capitalised intangibles	-8.4	-8.8	-6.0	-2.0	-1.0	0.0
Sale of fixed assets	0.0	0.0	0.0	0.0	0.0	0.0
Free cashflow	**-17.4**	**-13.2**	**-29.8**	**-17.8**	**-12.6**	**-7.0**
Acquisitions	0.0	0.0	0.0	0.0	0.0	0.0
Dividends	0.0	0.0	0.0	0.0	0.0	0.0
Investment in JVs	0.0	0.0	0.0	-3.0	0.0	0.0
Other investments	0.0	0.0	0.0	0.0	0.0	0.0
Cashflow after investments	**-17.4**	**-13.2**	**-29.8**	**-20.8**	**-12.6**	**-7.0**
Exercise of warrants	0.0	0.0	0.0	3.2	3.2	3.2
Equity issues	7.3	20.4	26.5	10.0	0.0	0.0
Currency effect	0.0	0.0	0.0	0.0	0.0	0.0
Cash/(debt) acquired	0.0	0.0	-8.6	0.0	0.0	0.0
Change in net debt	**-10.1**	**7.2**	**-11.9**	**-7.6**	**-9.4**	**-3.8**
OCFPS (p)	-11.4	-0.8	-10.3	-6.3	-4.3	-2.4
Opening net cash (debt)	0.9	-9.2	-2.0	-13.9	-21.5	-31.0
Closing net cash/(debt)	**-9.2**	**-2.0**	**-13.9**	**-21.5**	**-31.0**	**-34.7**

Source: Hardman & Co Life Sciences Research

Valuation

Outlook

Demand for PBT machines continues, with strong orders being reported throughout the precision radiotherapy industry over the past quarter. As of August 2019, IBA reported high levels of activity, with 10 rooms being delivered, on the back of a proton therapy market, which "continues to be solid". Varian reported a "strong growth in proton solutions" in its fiscal 4Q'19, which partly offset the fall in sales by 12% ($121.9m vs. $138.9m) for the whole year. Looking at the companies involved in traditional radiotherapy, the operating performance was more contrasted. Elekta reported very strong order intake in August 2019, associated with an increase in underlying profitability. Smaller players like Accuray and ViewRay, on the other hand, reported delays, which affected their performance.

Changes to share prices

Company	Ticker	9 May 2019	6 Nov 2019	Change
Accuray	ARAY.OQ	$4.20	$2.86	-32%
Advanced Oncotherapy	AVO.L	40.0p	38.5p	-4%
Elekta	EKTAB.ST	SKR115.4	SKr140.0	21%
IBA	IBAB.BR	€15.9	€ 14.70	-8%
Varian Medical Systems	VAR.N	$139.0	$124.4	-11%
ViewRay	VRAY.OQ	$8.46	$2.75	-67%

Source: Refinitiv, Hardman & Co Life Sciences Research

All our valuation tables have been updated to reflect current share prices, currencies, and the most recent financial reports from the various companies.

Peer group analysis

Although there are differences in the companies' activities compared with AVO, the following is considered to be the most constructive set of peers against which an informed view about the potential valuation of AVO can be made. AVO's quoted peers are trading on EVs that are multiples of that commanded currently by AVO – range 1.9x to 81.9x – as can be seen in the following table.

Peer group analysis

Company	Accuray	Advanced Oncotherapy	Elekta	IBA	Varian	ViewRay
Activity	Precision RT manufacturer	Linac PBT manufacturer	Linac RT manufacturer	Cyclotron PBT manufacturer	Linac RT & PBT synchrocyclotron	MR Linac manufacturer
Ticker	**ARAY**	**AVO**	**EKTAb**	**IBAB**	**VAR**	**VRAY**
Currency	$	£/p	SEK	€	$	$
Share price	2.86	38.5	140	14.7	124	2.80
Shares in issue (m)	88.8	237.6	518.4	30.1	90.8	98.5
Market cap (lc, m)	253.9	91.5	72,575	442.8	11,293	276
Mkt cap (£m)	196.2	91.5	5,867	382.1	8,727	213
Cash	76.8	8.7	4,118	20.3	531	92
Debt	-249.5	-22.6	-4,558	-78.4	-410	-69
EV (lc m)	426.6	105.4	73,015	500.9	11,171	253
EV (£m)	329.7	105.4	1,973	432.2	8,633	195
Relative EV	**3.1**	**-**	**18.7**	**4.1**	**81.9**	**1.9**

Prices and currencies taken at close of business on 6 November 2019
lc = local currency
Source: Hardman & Co Life Sciences Research

Traditional multiple-based valuations

Multiple-based valuation methodologies (P/E, EV/sales, EV/EBITDA) provide more information on the upside potential when LIGHT system sales commence.

Peer group valuation ratios

Company	Ticker	P/E			EV/sales			EV/EBITDA		
Year-end Dec		2018	2019E	2020E	2018	2019E	2020E	2018	2019E	2020E
Accuray*	ARAY	-12.2	-27.2	572.0	2.0	1.9	1.8	48.4	35.4	33.3
Advanced Oncotherapy	AVO	-2.7	-4.3	-4.6	-	-	4.9	-4.9	-5.6	-6.4
Elekta*	EKTAb	58.6	47.1	41.9	13.5	11.6	10.5	20.7	18.4	16.0
IBA	IBAB	17.1	6.8	17.3	2.4	2.0	1.8	63.9	52.4	38.3
Varian Medical Systems*	VAR	75.9	26.2	23.3	3.8	3.5	3.1	21.7	22.6	19.8
ViewRay	VRAY	-2.8	-2.2	-2.2	3.2	2.7	2.2	-3.6	-2.3	-2.2

**Ratios adjusted from reported to calendar year-end*
Based on share prices taken at close of business on 6 November 2019
Source: Hardman & Co Life Sciences Research

Company matters

Board of Directors

Board of Directors	
Name	**Position**
Dr Michael Sinclair	Executive Chairman
Nicolas Serandour	Chief Executive Officer
Prof. Steve Myers	Executive Director, ADAM executive Chairman
Michael Bradfield	Non-executive Director
Hans von Celsing	Non-executive Director
Chunlin Han	Non-executive Director
Dr Yuelong Huang	Non-executive Director
Dr Nick Plowman	Non-executive Director, Chairman Medical Advisory
Peter Sjostrand	Non-executive Director
Gabriel Urwitz	Non-executive Director
Dr Enrico Vanni	Non-executive Director
RenHua Zhang	Non-executive Director

Source: Company reports

Medical Advisory Board

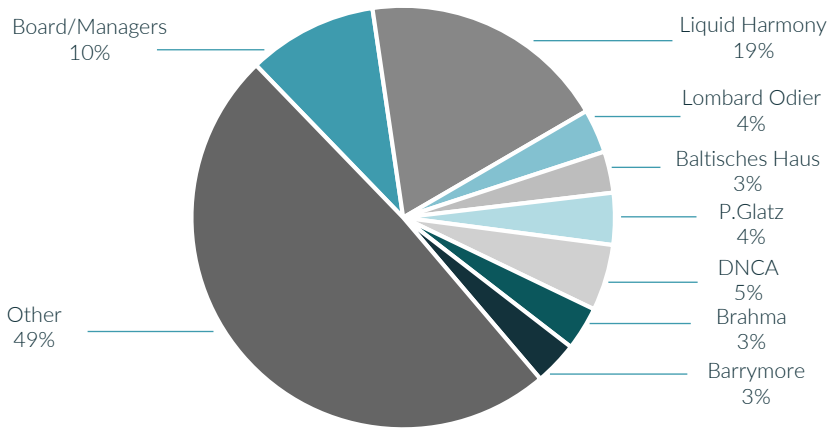
Medical Advisory Board	
Name	**Affiliation**
Prof. Ugo Amaldi	Founder and President of the TERA Foundation
Dr Hanne Kooy	Associate Director of Medical Physics at Harvard Medical School
Dr Jay S Loeffler	Professor of Radiation Oncology at Harvard Medical School and Chair of Radiation Oncology at the Massachusetts General Hospital
Prof. Chris Nutting	Clinical oncologist & chair at The Royal Marsden and ICR London
Dr Margaret Spittle OBE	Clinical oncologist at University College Hospital London
Dr Euan Thomson	Operating partner at Khosla Ventures, CEO of AliveCor and Director of the Hospice of the Valley

Source: Company reports

Share capital

There are 237,592,656 Ordinary shares in issue. In addition, there are currently 7.7m options and 34.3m warrants outstanding.

Shareholders



Source: Company announcements, Hardman & Co Life Sciences Research

Appendix

Competitive landscape with respect to FLASH

The leading PBT manufacturers claim that they are FLASH-ready and pre-clinical studies are taking place. This has to be nuanced as the machine they use needs to be customised for the experiment itself. More importantly, FLASH needs to be delivered at all energies, and not just one single maximum energy that is required to treat a deep-seated tumour. It is unclear from the studies performed whether competitors of AVO can deliver FLASH at all energies, due to the technical design of their systems.

IBA

IBA claims to be FLASH-capable and has filed its first patent related to FLASH in 2010. IBA is collaborating with several leading proton therapy centres to better understand the mechanisms of FLASH irradiation. This early development work enables IBA to deliver FLASH irradiation on both its current single and multi-room proton therapy platforms in a clinical environment, but the technique is not commercially available.

In March 2019, IBA announced the first FLASH irradiation in an IBA gantry treatment room at the University Medical Centre Groningen in The Netherlands, using a ProteusPLUS machine with a dose rate of up to 200 Gy/s.

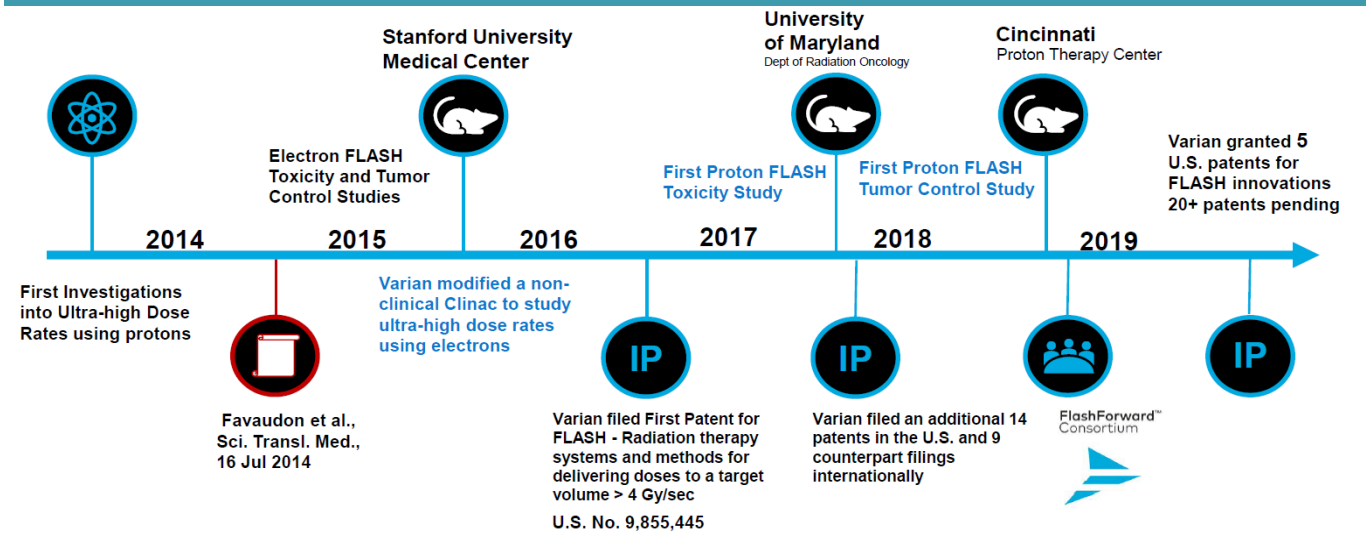
A second experiment took place at the Rutherford Cancer Centre Thames Valley in Reading (UK) on 8 June 2019 using a ProteusONE compact gantry treatment room.

At the recent PTCOG meeting in September 2019, IBA shared its latest research on FLASH radiotherapy for gastrointestinal malignancy, performed at the Perelman School of Medicine, University of Pennsylvania, Philadelphia.

Varian

Varian has been working on the FLASH hypothesis since 2014 in collaboration with the University of Maryland School of Medicine and performed the first animal study in 2016 using a its ProBeam system.

Varian's FLASH timeline



Source: Varian 2019 PTCOG presentation

Mevion

Mevion teamed up the Washington University School of Medicine in St. Louis to study FLASH therapy and if this technique could be applied with Mevion's machines. In a recent experiment, a research team was able to deliver dose rates of 226 Gy/s on a production machine, well above the threshold for the FLASH regime of 40 Gy/s shown in pre-clinical studies, and drastically higher than traditional proton therapy delivery rates of 2 Gy/s. It is also investigating new dosimetry instrumentation to better handle real-time measurements of such ultra-high dose regimes.

https://www.mevion.com/newsroom/press-releases/focus-future-flash-therapy

Hitachi

Hitachi has not indicated if it is investigating FLASH technology. It is possible that it is working undercover and simply not made any public statements or presented at any conferences.

References

1. Particle Therapy Co-Operative Group https://www.ptcog.ch/

2. *Commercialising a breakthrough technology*, Hardman & Co. 13 May 2019. https://www.hardmanandco.com/wp-content/uploads/2019/05/AVO-%E2%80%93-Is-PT-the-new-MRI-13-May-2019.pdf

3. NHS England clinical commissioning policy: *Proton beam therapy for children, teenagers and young adults in the treatment of malignant and non-malignant tumours*, July 2018, reference 1783. https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2019/07/Interim-Policy-PBT-for-CTYA-for-malignant-and-non-malignant-tumours.pdf

4. Bourhis, J., Sozzi, WJ., Gonçalves Jorge, P., Gaide, O., Bailat, C., Duclos, F., Patin, D., Ozsahin, M., Bochud, F., Germond, J-F., Moeckli, R and Vozenin, M-C. *Treatment of a first patient with FLASH-radiotherapy*, Radiotherapy & Oncology, 2019, 139, 18–22.

Glossary

AAPM	American Association of Physicists in Medicine
CCL	Coupled Cavity Linac – accelerate the proton beam to the clinically relevant energy
CERN	Conseil Européen pour la Recherche Nucléaire
CMS	US Centers for Medicare & Medicaid Services
CBSA	Core-Based Statistical Area
FLASH	Delivery of ultra-high radiation dose of an entire therapy session in a single flash lasting less than a second
HOPD	Hospital Outpatient Department
Hypo-fractionation	Delivery of higher doses of radiation in fewer fractions than are used in conventional radiation therapy.
Linac	Linear accelerator
MeV	Mega-electron Volts
PBT	Proton Beam Therapy
PTCOG	Particle Therapy Co-Operative Group
RFQ	Radio Frequency Quadruple – focuses the proton beam and accelerates the protons up to 5MeV
RT	Radiotherapy
SCDTL	Side Coupled Drift Tube Linac – low-speed accelerating units that accelerate the protons from 5MeV to 37.5MeV
STFC	Science and Technology Facilities Council

Disclaimer

Hardman & Co provides professional independent research services and all information used in the publication of this report has been compiled from publicly available sources that are believed to be reliable. However, no guarantee, warranty or representation, express or implied, can be given by Hardman & Co as to the accuracy, adequacy or completeness of the information contained in this research and they are not responsible for any errors or omissions or results obtained from use of such information. Neither Hardman & Co, nor any affiliates, officers, directors or employees accept any liability or responsibility in respect of the information which is subject to change without notice and may only be correct at the stated date of their issue, except in the case of gross negligence, fraud or wilful misconduct. In no event will Hardman & Co, its affiliates or any such parties be liable to you for any direct, special, indirect, consequential, incidental damages or any other damages of any kind even if Hardman & Co has been advised of the possibility thereof.

This research has been prepared purely for information purposes, and nothing in this report should be construed as an offer, or the solicitation of an offer, to buy or sell any security, product, service or investment. The research reflects the objective views of the analyst(s) named on the front page and does not constitute investment advice. However, the companies or legal entities covered in this research may pay us a fixed fee in order for this research to be made available. A full list of companies or legal entities that have paid us for coverage within the past 12 months can be viewed at http://www.hardmanandco.com/legals/research-disclosures. Hardman may provide other investment banking services to the companies or legal entities mentioned in this report.

Hardman & Co has a personal dealing policy which restricts staff and consultants' dealing in shares, bonds or other related instruments of companies or legal entities which pay Hardman & Co for any services, including research. No Hardman & Co staff, consultants or officers are employed or engaged by the companies or legal entities covered by this document in any capacity other than through Hardman & Co.

Hardman & Co does not buy or sell shares, either for their own account or for other parties and neither do they undertake investment business. We may provide investment banking services to corporate clients. Hardman & Co does not make recommendations. Accordingly, they do not publish records of their past recommendations. Where a Fair Value price is given in a research note, such as a DCF or peer comparison, this is the theoretical result of a study of a range of possible outcomes, and not a forecast of a likely share price. Hardman & Co may publish further notes on these securities, companies and legal entities but has no scheduled commitment and may cease to follow these securities, companies and legal entities without notice.

The information provided in this document is not intended for distribution to, or use by, any person or entity in any jurisdiction or country where such distribution or use would be contrary to law or regulation or which would subject Hardman & Co or its affiliates to any registration requirement within such jurisdiction or country.

Some or all alternative investments may not be suitable for certain investors. Investments in small and mid-cap corporations and foreign entities are speculative and involve a high degree of risk. An investor could lose all or a substantial amount of his or her investment. Investments may be leveraged and performance may be volatile; they may have high fees and expenses that reduce returns. Securities or legal entities mentioned in this document may not be suitable or appropriate for all investors. Where this document refers to a particular tax treatment, the tax treatment will depend on each investor's particular circumstances and may be subject to future change. Each investor's particular needs, investment objectives and financial situation were not taken into account in the preparation of this document and the material contained herein. Each investor must make his or her own independent decisions and obtain their own independent advice regarding any information, projects, securities, tax treatment or financial instruments mentioned herein. The fact that Hardman & Co has made available through this document various information constitutes neither a recommendation to enter into a particular transaction nor a representation that any financial instrument is suitable or appropriate for you. Each investor should consider whether an investment strategy of the purchase or sale of any product or security is appropriate for them in the light of their investment needs, objectives and financial circumstances.

This document constitutes a 'financial promotion' for the purposes of section 21 Financial Services and Markets Act 2000 (United Kingdom) ('FSMA') and accordingly has been approved by Capital Markets Strategy Ltd which is authorised and regulated by the Financial Conduct Authority (FCA).

(Disclaimer Version 8 – Effective from August 2018)

research@hardmanandco.com

35 New Broad Street
London
EC2M 1NH

+44(0)20 7194 7622

www.hardmanandco.com