Accelerators at IBA

June 2019
An alternative offer?

Many others available…!
## An alternative offer?

<table>
<thead>
<tr>
<th></th>
<th>HL-LHC</th>
<th>FCC-hh</th>
<th>Kiube</th>
<th>Cyclone 70</th>
<th>Cyclone 230</th>
<th>S2C2</th>
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<tr>
<td>Beam energy (TeV)</td>
<td>7</td>
<td>50</td>
<td>1,80E-05</td>
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<td>2,30E-04</td>
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<td>~60</td>
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<tr>
<td>RMS IP spot size (µm)</td>
<td>7,1</td>
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So... What do you think?
So… What do you think?
IBA today

- A world leading innovator in cancer diagnostics and treatment
  - Number one provider of proton therapy solutions
  - Global leader in RadioPharma and Industrial Solutions

- 1,400 employees worldwide

- Most advanced PT offering
  - Single and multi room systems equipped with cutting edge technology

Proteus®ONE and Proteus®PLUS are brand names of Proteus 235

*December 2018
With IBA dosimetry
Outline

What we do and a few interesting things from our applications

- Protontherapy Systems and some highlights
- Radiopharmaceutical Solutions and Theranostics
- Industrial Applications and system Flexibility
- Final thoughts
Proton Therapy
Most conventional radiation therapy and arc therapy systems use xrays of a few MeV for cancer treatment

- Dose is not delivered to tissues by the photons themselves, but rather through secondary electrons produced by 3 mechanisms

G.F. Knoll – Radiation detection and measurement, Wiley
« Conventional » Radiation Therapy vs. Hadrontherapy

- Results in:
  - A decrease of photon numbers following a superimposition of decreasing exponentials
  - electron buildup

=> dose builds-up and then ~exponentially decreases with depth once electron equilibrium is reached
Conventional Radiation Therapy vs. Hadrontherapy

- Instead, hadrons lose their energy in matter according to Bethe-Bloch formula:

\[
-\frac{dE}{dx} = 2\pi N_A r_e^2 m_e c^2 \rho \frac{Z}{A} \frac{z^2}{\beta^2} \left[ \ln \left( \frac{2m_e \gamma^2 v^2 W_{\text{max}}}{I^2} \right) - 2\beta^2 - \delta^2 - \frac{C}{Z} \right]
\]

Where

\[W_{\text{max}} = \frac{2m_e c^2 \beta^2 \gamma^2}{1 + 2 \frac{m_e}{M} \sqrt{1 + \left( \frac{m_e}{M} \right)^2 + \beta^2 \gamma^2}} \approx 2m_e c^2 \beta^2 \gamma^2\]

is head-on collision energy transfer

And

\[I(eV) = Z \left( \frac{12}{Z} + \frac{7}{Z} \right) \quad \text{for } Z < 13\]
\[I(eV) = Z \left( 9.76 + 58.8Z^{-1.19} \right) \quad \text{for } Z \geq 13\]

is the average ionization potential of the absorber

And

\[Z \rightarrow Z_{\text{eff}} = \sum a_i Z_i\]
\[A \rightarrow A_{\text{eff}} = \sum a_i A_i\]
\[\ln(I) \rightarrow \ln(I_{\text{eff}}) = \sum \frac{a_i Z_i \ln(l_i)}{Z_{\text{eff}}}\]
\[\delta \rightarrow \delta_{\text{eff}} = \sum \frac{a_i Z_i \delta_i}{Z_{\text{eff}}}\]
\[C \rightarrow C_{\text{eff}} = \sum a_i C_i\]
In short, it results in the famous « bragg peak » dose distribution.
Dose Conformation

Protons:
- Minimal radiation exposure of healthy organs
- Potential to reduce the risk of secondary cancers
- Potential to improve the quality of life for patients during and after treatment
- Possibility of retreatment
What does a system look like?

Proteus® PLUS

1800 m²

Proteus® ONE

360 m²

- Permanent Magnet
- Constant Energy
- High Current
- Continuous Beam
- Cyclotron

- PBS with Variable Spot
- Size App's & Comp's
- 0.5 sec Layer Change

- Dual Energy CBCT
- Integrated with Positioner
- 5 RPM, Spiral Capable

- Dual Energy Selection Systems
- < 1 sec Room Switching

- 360° Superconducting Gantry

- Auxiliary Positioner
- Calibration PET at isocenter
What does a system look like?

Compact super-conducting accelerator for producing the energetic proton beam

A rotating gantry to set the beam at the right angle

Intensity-modulated proton therapy (IMPT): the most precise form of treatments

Stereoscopic imaging and CBCT at isocentre: accurate patient setup, quality images for adaptive treatments

Efficient software integration, enabling easy & flexible workflows
Accelerators – (Synchro-)Cyclotrons

Max. energy = 160 MeV
Avg. power = 250 KW
COST = 0.75 Million (1948$)

(L) Dr. Lee Davenport (R) Dr. Norman Ramsey
June 10 1949
Accelerators – (Synchro-)Cyclotrons

- **IBA C230**
  - 230 MeV protons
  - 4.3 m Diameter
  - CW beam
  - Normal conducting
  - Magnet: 200 kW
  - RF: 60 kW

- **Varian-Accel Probeam**
  - 250 MeV protons
  - 3.1 m Diameter
  - CW beam
  - Superconducting (NbTi)
  - Magnet: 40 kW
  - RF: 115 kW

- **Mevion SC250**
  - 250 MeV protons
  - ~1.5 m Diameter (shield)
  - Superconducting (Nb3Sn)

- **IBA S2C2**
  - MeV protons
  - 2.2 m Diameter
  - Rep. rate: 1 kHz
  - Superconducting (NbTi)
  - RF: 11 kW
Accelerators - Ongoing developments

1. Isochronous: SHI, Varian/Antaya, Pronova/Ionetix, Heifei/JINR

**SHI**
- 230 MeV protons
- 2.8 m Diameter
- CW beam
- Superconducting (NbTi)
- 65 tons
- 4 T (extr.)

**Pronova/Ionetix**
- 250 MeV protons
- 2.8 m Diameter
- CW beam
- Superconducting (Nb$_3$Sn)
- 60 tons
- 3.7 T (extr.)

**Heifei/JINR**
- 200 MeV protons
- 2.2 m Diameter
- CW beam
- Superconducting
- 30 tons
- 3.6 T (extr.)

**Varian/Antaya**
- 230 MeV protons
- 2.2 m Diameter
- CW beam
- Superconducting (Nb$_3$Sn)
- 30 tons+
- 5.5 T (extr.)
- “Flutter” coils
Dealing with the Limitations of Iron-Dominated Magnets

- Flutter coils are useful to overcome the limitation of iron-dominated field variation

- Same concept can be used for extraction systems

- Limitations:
  - Adds complexity (cryogenics closer to median plane)
  - Less sharp field variations
Proton cyclotrons - Ongoing developments

- 2. Synchrocyclotrons: MIT ironless (Pronova)

- 250 MeV protons
- (2.4-)2.8 m Diameter
- Pulsed beam
- Superconducting (Nb₃Sn)
- 4 tons
- T (extr.)
- Cost?
- Variable-energy possible
Is it worth increasing the field to high values?

- Lower weight helps but is not always an issue (i.e. iron is cheap), as long as you stay within certain limits.
- Size matters: facility footprint vs. accelerator complexity (turn sep.)
Smaller Gantries (carbon)

- **Further size reduction** (despite downstream scanning: almost smaller than Pronova proton gantry! At high field and same scanning option… SAD sets system size)
- **Less cryogenics needs** (from 34 to 9-12 cryocoolers)

NB: remember carbon is even more of a niche than PT, with mostly research institutes involved…
Brand New gantry concepts

GaToroid for C-ions

- Number of coils: 16 (-)
- Ampere-turns: 3 (MA-turns)
- Peak Field on coil: 13.8 (T)
- Coil dimension: ~3 x 2 (m x m)
- Torus dimensions: ~3 x 5 (m x m)

**Estimated mass: ~50 (tons)**
- Total Stored energy: 370 (MJ)
- Operating current: 6 (kA)
  - $J_E = 200...300$ (A/mm$^2$)
- Coil Inductance: 0.3 (H)

Operating Temperature
- 4.5 K (LTS)
- 10 K (HTS)

There is quite some work to be done here...
Most Exciting things today in PT

- Cost and adoption => Model-based approach
- Better sparing of healthy tissues => Arc Therapy and/or Flash
Irradiation of surrounding tissues - Hepatocellular carcinoma

“PBT was found to be a safe and effective local-regional therapy for inoperable HCC. A randomized controlled trial to compare its efficacy to a standard therapy has been initiated” (*)

<table>
<thead>
<tr>
<th>Tissues</th>
<th>Photons</th>
<th>Protons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right Kidney</td>
<td>20 Gy</td>
<td>0.1 Gy</td>
</tr>
<tr>
<td>Lung</td>
<td>12.5 Gy</td>
<td>8.5 Gy</td>
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Pediatric medulloblastoma – Side effects (NTCP)

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<tr>
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<th>Protons</th>
<th>Photons</th>
</tr>
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<tbody>
<tr>
<td>Restrictive Lung Disease</td>
<td>0%</td>
<td>60%</td>
</tr>
<tr>
<td>Reduced exercise capability</td>
<td>0%</td>
<td>75%</td>
</tr>
<tr>
<td>Abnormal EKGs</td>
<td>0%</td>
<td>31%</td>
</tr>
<tr>
<td>Growth abnormality</td>
<td>20%</td>
<td>100%</td>
</tr>
<tr>
<td>IQ drop of 10 points at 6 yrs</td>
<td>1.6%</td>
<td>28.5%</td>
</tr>
<tr>
<td>Risk of IQ score &lt; 90</td>
<td>15%</td>
<td>25%</td>
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</table>

“Proton beam therapy has become a standard of care for pediatric cancers…” (*)

(*) Presentation Dr. Jay S. Loeffler, NPTC/MGH, ASTRO 2001
Adoption => Model-based approach

https://doi.org/10.1016/j.radonc.2013.05.007
Adoption => Model-based approach

**NO PROTONS AVAILABLE**

Historical control group treated with photons

- All treated with PHOTONS
  - PHOTON treatment plan
- Back up PROTON plan

**PROTONS AVAILABLE**

Group treated with PROTONS (only if estimated NTCP-reductions > threshold)

- All treated with PHOTONS
  - PHOTON treatment plan
- Back up PROTON plan
- PROTON treatment plan

Group not selected for protons and treated with PHOTONS (because estimated NTCP-reductions remains BELOW threshold)

- All treated with PHOTONS
  - PHOTON treatment plan

Comparison

Treatment outcome with PHOTONS with estimated NTCP-reductions BELOW threshold (NO controls)

**https://doi.org/10.1016/j.radonc.2013.05.007**
Trends in PT - Proton Arc therapy

- **Spot-Scanning Proton Arc therapy**
  - Enhances dose conformity at the tumor level
  - Reduces the total dose received by the patient
  - Increases the robustness of the treatment plan
  - Improves the adoption of dose escalation and hypofractionation

- **Proton Arc therapy proof of concept**
  - In collaboration with Beaumont Health Proton Therapy Center in Royal Oak, Michigan. Plan delivered in August 2018

Brain SRS
First irradiation of a proton ARC beam

- World première in proton therapy
- Plan delivered in August 2018

THE FIRST IRRADIATION OF A PROTON ARC BEAM

In collaboration with Beaumont Health Proton Therapy Center
Flash could allow dose escalation with less complications
- IBA’s equipment is Flash ready
- IBA is the only company to have demonstrated Flash compatible dose rate in a clinical environment (at UMCG in Groningen on March 1 2019 AND in Reading on June 8 2019 – videos on Youtube)
### Radiopharmaceuticals

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<td>7,1</td>
<td>6,8</td>
<td>2000</td>
<td>2000</td>
<td>3000</td>
<td>3000</td>
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RadioPharma Solutions

Tailor made radiopharmaceutical production centers

SYNTHERA®

CYCLONE® KIUBE

INTEGRALAB®

More than 500
Synthera worldwide

Cyclotrons sold

Middle and High energy
RadioPharma Solutions

- New generation Cyclone®KIUBE and Cyclone®70
  - Reach new markets
  - Gain market shares
  - Give access to latest applications (e.g. theranostics)

- High energy and high current proton cyclotron
- Production of isotopes for diagnosis of cardiovascular diseases and other critical illnesses

- Highest radiopharmaceuticals production capacity
- Upgradable to enable the increase of production capacity
- Give access to 18F, 13N, 15O, 11C (CO2 & CH4), 18F2, 68Ga,...
Most exciting thing in RPS today: Theranostics

- Is there a tumor?
- Is it solitary or metastatic?
- Has the tumor the right receptors for efficient therapy?
- Therapy: same molecule with therapy isotope.
## Exciting for IBA: Cyclotron or Rhodotron-based Production

### Radiometals

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Half life (h)</th>
<th>Mode (keV)</th>
<th>Production</th>
<th>Chelator</th>
<th>Diagnostic match</th>
<th>Half life (h)</th>
<th>Production</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{90}$Y</td>
<td>64.1</td>
<td>$\beta^-$ (934)</td>
<td>Generator</td>
<td>DTPA (tiuxetan) DOTA</td>
<td>$^{68}$Ga, $^{86}$Y $^{111}$In</td>
<td>1.13 (PET) 14.7 (PET) 67.9 (SPECT)</td>
<td>Generator Cyclotron Cyclotron</td>
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<tr>
<td>$^{177}$Lu</td>
<td>161</td>
<td>$\beta^-$ (134) $\gamma$ (112, 208)</td>
<td>Reactor</td>
<td>DOTA</td>
<td>$^{68}$Ga $^{111}$In</td>
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<tr>
<td>$^{67}$Cu</td>
<td>61.9</td>
<td>$\beta^-$ (141) $\gamma$ (91, 93, 185)</td>
<td>Cyclotron</td>
<td>NOTA NODAGA TETA CPTA (DOTA) cross-bridged macrocycles</td>
<td>$^{64}$Cu $^{62}$Cu $^{61}$Cu</td>
<td>12.9 (PET) 0.16 (PET) 3.3 (PET)</td>
<td>Cyclotron (Generator)</td>
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<tr>
<td>$^{47}$Sc</td>
<td>80.4</td>
<td>$\beta^-$ (162) $\gamma$ (159)</td>
<td>Various</td>
<td>DOTA AAZTA DO3AP</td>
<td>$^{86}$Y $^{43}$Sc $^{44}$Sc</td>
<td>14.7 (PET) 3.9 (PET) 3.97 (PET)</td>
<td>Cyclotron Generator</td>
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« Exciting » for the Patient: Prostate cancer

SNMMI 2018 Image of the year

$^{68}$Ga-PSMA PET before and after $^{177}$Lu PSMA617 theranostic in 8 patients with metastatic prostate cancer
## Industrial Solutions

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Industrial Solutions

Sterilization and polymer improvement solutions

RHODOTRON®

DYNAMITRON®

World No. 1

250 IBA Industrial accelerators
Exciting stuff in these applications

Well, maybe there are too many exciting tings, and it is sometimes hard to distinguish what will become big or not

But:

- Variety in applications
  - Accelerator versatility
    - Energy
    - Current
    - Beam lines
The Rhodotron

- CEA patent brought to market by IBA
  - From the TT50 (20 kW, 10 MeV)
  - To the TT1000 (800 kW, 7 MeV)
  - To the TT300HE (120 kW, 40 MeV)
- Pulsed operation for energy-saving
Flexibility: Energy

- This layout allows to extract two different energies onto one same target
  - first 4 passes accelerate up to 5.8 MeV
  - magnet 5 on
    - last pass accelerates up to 6.96 MeV
  - magnet 5 off:
    - beam passes through delay magnet
    - the beam is reinjected into the same final pass but the RF-phase is shifted
    - last pass can accelerate (1.16 MeV) or decelerate or anything in between depending on the position of the delay magnet
  - two solutions exist for each extraction energy

- 5 MeV layout may replace dynamitron

Idea of Michel Abs
Flexibility: Beam Power => Solid-State RF amplifiers

- Frequencies: 40, 106, 176, 352 MHz
- Power: from 10 kW to...
IBA strong purpose – 5 stakeholders

- Affordability
- Treatment & Process
- Quality
- Innovation
- Customer Satisfaction

- Profitability
- Ownership & Independence
- Access to good capital

- Quality Jobs
- The Promise
- Health & Safety

- Business Ethics
- Responsible Procurement
- Education
- Community involvement

- Climate Change
- Waste
- Mobility
- Resources scarcity
Protect, Enhance and Save Lives

Thank you

(and if you happen to come back to Belgium, come and visit us…)

Viggo Mommaerts, treated with Proton Therapy