10 reasons why you should consider proton therapy for your radiation oncology department

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10 reasons why you should consider proton therapy

1. Physics of Protons
2. Become a Leading Center
3. Expanding Indications
4. Proper Patient Selection
5. Large Patient Population
6. Be an Innovator
7. More Compact and Affordable Solutions
8. High Throughput
9. Participate in Clinical Trials
10. Fast Installation Time

**23%**

23% of patients are treated using proton therapy in centers who are equipped with both photon and proton therapy.*

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**Abbreviated 2017 Report**
Physics of protons leads to benefits for the patients for certain indications
The Bragg peak

- 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

*The proton beams release most of their energy inside a reduced area at the heart of the tumor, depositing a lower entry dose and no exit dose.*
Standard radiotherapy and proton therapy

**Standard Radiotherapy**

- **Entry dose**
- **Exit dose**

**Proton Therapy**

- **Entry dose**

 Deposits most of its energy in front of the tumor

 Deposits most of its energy inside the tumor
Potential benefits of proton therapy for the patients

- Improvement of local control
- Reduce side effects
- Lower risk of secondary cancers
- Treatment of choice for re-irradiation
Example of dosimetric comparison for pediatric patients

More information about pediatric cancer in white papers, reference 1, 2, 3

Courtesy of Seattle Cancer Care Alliance Proton Therapy Center - Medulloblastoma
Example of dosimetric comparison for lung cancer

More information about lung cancer in white papers, reference 1, 2

Photons

Protons

Courtesy of Seattle Cancer Care Alliance Proton Therapy Center – Non-Small Cell Lung Cancer
Example of dosimetric comparison for left breast cancer

More information about breast cancer in white papers, reference 1, 2

Courtesy of Seattle Cancer Care Alliance Proton Therapy Center – Locally Advanced Stage III Breast Cancer
How does that reflect to your patient for a Head & Neck patient?

More information about head & neck cancers in white papers, reference 1, 2, 4

Photons

Protons

Photons-Protons excess
Up to 25 Gy

Courtesy of Dr Nancy Lee, MSKCC
What unnecessary radiation means for the patient

25 Gy

What is a Gray (Gy)?
It is a measure of absorbed radiation dose.

12,500
Head & Neck CTs
(2mSv)

5,000,000
Intraoral X-Rays
(0.002mSv)

25,000x
General Public's Annual Limit
(1.0mSv)

+96%
Secondary Cancer Risk
(12,500 CTs, 60 yo)

Courtesy of Dr Steven Frank, MD Anderson Cancer Center
Become a leading center and join the growing clinical institutions that chose to offer proton therapy to their patients
The number of proton therapy centers* is growing fast

* Include research and academic centers. See the list of centers in annex.
Worldwide proton therapy institutions including research

North America
- Centers: 41
- Rooms: 110

EMEA, Latin America, Russia CIS
- Centers: 49
- Rooms: 94

Asia Pacific
- Centers: 44
- Rooms: 105

309 rooms
134 centers

* Include research and academic centers. See the list of centers in annex.
Proton institutions in North America

41 Total centers
29 Centers in operation

110 Total rooms
85 Rooms in operation

* Include research and academic centers. See the list of centers in annex.
Proton institutions in EMEA, Latin America and Russia-CIS

- Total centers: 49
- Centers in operation: 26
- Total rooms: 94
- Rooms in operation: 54

* Include research and academic centers. See the list of centers in annex.
Proton institutions in Asia pacific

- Total centers: 44
- Centers in operation: 19
- Total rooms: 105
- Rooms in operation: 46

* Include research and academic centers. See the list of centers in annex.
Indications are expanding and national and regional associations are updating their guidelines and recommendations.
Extension of the indications treated with Pencil Beam Scanning

**Typical cancer indications treated (% patients)**  
(data from a leading center in the US)
Guidelines and recommendations are updated in North America

Central Nervous System Cancers
It is reasonable to consider proton beam for craniospinal irradiation where available as it is associated with less toxicity.

Head and Neck Cancers
IMRT or other conformal techniques (3-D conformal, helical tomotherapy, VMAT, and proton beam therapy [PBT]) may be used as appropriate depending on the stage, tumor location, physician training/experience, and available physics support.

Non-Small Cell Lung Cancer
More advanced technologies are appropriate when needed to deliver curative RT safely. These technologies include (but are not limited to) 4D-CT and/or PET/CT simulation, IMRT/VMAT, IGRT, motion management, and proton therapy.

Hepatocellular Carcinoma
Proton beam therapy (PBT) may be appropriate in specific situations.

Eosophagial and Esophagogastric Junction Cancers
Intensity-modulated radiation therapy (IMRT) or proton beam therapy is appropriate in clinical settings where reduction in dose to organs at risk (eg. Heart, lungs) is required that cannot be achieved by 3-D techniques.

More information about NCCN in reference 8, and ASTRO in reference 9

ASTRO updates insurance coverage recommendations for proton therapy

ARLINGTON, Va., July 13, 2017

Proton beam therapy model policy recommends expanded access to advanced radiation therapy treatment for cancer patients

The American Society for Radiation Oncology (ASTRO) has issued an update to its recommendations for medical insurance coverage regarding the use of proton beam therapy to treat cancer. The updated Proton Beam Therapy Model Policy provides guidance to payers on clinical indications that are appropriate for treatment with proton therapy and should be covered by health insurance, including Medicare, Medicaid and private insurance.
Recognition of the clinical advantages of proton therapy

Types of cancer for which clinical trials using proton therapy treatment are being conducted

- Lymphoma: 2%
- Uterine: 2%
- Anus: 2%
- Liver: 3%
- Sarcoma: 6%
- Pancreas: 6%
- Esophagus: 8%
- Head and Neck: 11%
- Breast: 14%
- Gastro-intestine: 1%
- Reirradiation: 3%
- Others: 14%
- Brain / Central Nervous System / Base of skull: 24%
- Pediatric: 23%
- Eye: 4%
- Prostate: 21%
- Lung: 16%

629
Scientific articles published in 2017

160
Trials ongoing as of the end of 2017

More information about clinical trials in reference 7 and clinical papers in reference 1
Selecting the patients that could benefit most from proton therapy can be eased thanks to the model-based approach.
Model-based approach to select the patients

3 steps to select patients that will most likely benefit from protons compared to photons in terms of Normal Tissue Complication Probability (NTCP) value reductions

1. Select NTCP models in patients treated
2. Individual dose comparison
3. Estimation of NTCP reduction

More information about Model-Based Approach in reference 14, 15

Courtesy of Dr Johannes Langendijk, UMCG
Example for head and neck cancer

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2. Individual dose comparison
3. Estimation of NTCP reduction

More information about Model-Based Approach in reference 14, 15

Courtesy of Dr Johannes Langendijk, UMCG
First experience at UMCG

Model-based patient selection
First experience at GPTC (since February 2018)

More information about Model-Based Approach in reference 14, 15

Courtesy of Dr Johannes Langendijk, UMCG
Over 180,000 estimated patients were treated with proton therapy. According to survey, 23% of patients are treated with proton therapy in centers that are equipped with both photon and proton therapy.
Over 180,000 estimated patients were treated with PT

Accumulated patients treated

Trends

More information about PTCOG patient statistics in reference 5
Who could benefit from proton therapy?

- <1% Today
- 17.7% Following reports*
- 23% Survey** among US RT centers with PT

*Extrapolation from the Dutch report
**Alcimed report 2017

More information about Dutch Report in reference 6
Indications potentially benefitting from PT according to the “Dutch Report”

<table>
<thead>
<tr>
<th>Indications</th>
<th>Standard (0,6% of RT)</th>
<th>Improved local control (3%)</th>
<th>Reduced side effects (12,1%)</th>
<th>Reduced secondary cancers (2%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pediatric</td>
<td>X</td>
<td></td>
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<tr>
<td>Brain</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base of skull</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intracranial</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Head &amp; Neck</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
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<tr>
<td>Urologic</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Lung</td>
<td></td>
<td>X (NSCLC)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Sarcoma</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Re-irradiation</td>
<td></td>
<td>X</td>
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<td>Breast</td>
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<tr>
<td>Testis</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
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</tbody>
</table>

17.7% of RT patients could benefit from PT from an extrapolation of the Dutch report

More information about Dutch Report in reference 6
Estimated number of proton therapy rooms needed worldwide

- **Gap analysis based on IBA internal modelling with 17.7% of RT patients that could benefit from protons**
- **Over 2000 proton rooms needed**

More information about Dutch Report in reference 6
Be an innovator and use the latest technologies in proton therapy including PBS, CBCT and systems to treat moving targets
The advantages of modern pencil beam scanning

- Improved conformity (e.g. concave dose distribution)
- Faster delivery
- Less hardware
- Fewer neutrons
- Intensity-modulation
- Gradient matching for LARGE fields
- Structure & Metal avoidance
- Multiple targets
- FAST Layer- & Volumetric RE-painting

More information about PBS and CBCT in reference 17

Courtesy of Andrew Lee, Texas Center for Proton Therapy
Comparison with other techniques

<table>
<thead>
<tr>
<th></th>
<th>2 D X-rays</th>
<th>3 D X-rays</th>
<th>IMRT</th>
<th>CONVENTIONAL PROTONS (Passive-scattered)</th>
<th>IMPT intensity modulated proton therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conformity</td>
<td>+</td>
<td>++</td>
<td>++++</td>
<td>++++ 1/2</td>
<td>++++</td>
</tr>
<tr>
<td>Normal tissue exposure</td>
<td>+++</td>
<td>+++</td>
<td>++++</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>

More information about PBS and CBCT in reference 17

Courtesy of Andrew Lee, Texas Center for Proton Therapy
Example with breast cancer

More information about PBS and CBCT in reference 17

Courtesy of Andrew Lee, Texas Center for Proton Therapy (TCPT)
Example with cranio-spinal

Cranio-spinal radiation therapy with gradient matching using IMPT (virtual “dose-feathering”) Faster and safer

More information about PBS and CBCT in reference 17

Courtesy of Andrew Lee, Texas Center for Proton Therapy (TCPT)
On-board CBCT helps with volumetric image guidance

Courtesy of Andrew Lee, Texas Center for Proton Therapy (TCPT)
Imaging systems in a Proteus®ONE

**kV-kV stereoscopic imaging**
- Instantaneous
- More precise
- Available for most of gantry and couch positions

**On-board Cone-beam CT**
- At isocenter
- LFOV (47cm x 26cm)
- Adaptive ready
Imaging at WKCC

WKCC Experience Summary

- CBCT
  - essential for H/N, thorax, abdomen, pelvis (prostate bed)
  - LFOV is useful for breast, pelvis
- Stereo Oblique
  - Bony structure
  - Fiducials

More information about CBCT in reference 18

Courtesy of Gwen Chen, Willis-Knighton Cancer Center (WKCC)
## Current imaging clinical applications at WKCC

<table>
<thead>
<tr>
<th>Site</th>
<th>Stereo Oblique</th>
<th>CBCT</th>
<th>2D Orthogonal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td>V</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Head/Neck</td>
<td>V</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Thorax/Lung</td>
<td>V</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Thorax/Lung (BH)</td>
<td>V</td>
<td>A*</td>
<td>A</td>
</tr>
<tr>
<td>Breast/ Chest Wall</td>
<td>V</td>
<td>A</td>
<td>--</td>
</tr>
<tr>
<td>Abdomen (BH)</td>
<td>V</td>
<td>A*</td>
<td>A</td>
</tr>
<tr>
<td>Pelvis</td>
<td>V</td>
<td>A</td>
<td>--</td>
</tr>
<tr>
<td>Prostate</td>
<td>A &amp; V</td>
<td>A (weekly)</td>
<td>--</td>
</tr>
<tr>
<td>Prostate Bed</td>
<td>V</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Extremities</td>
<td>V</td>
<td>A</td>
<td>A</td>
</tr>
</tbody>
</table>

- **A**: Patient Position Alignment  
- **V**: Patient Position Verification  
- **not used clinically**

More information about CBCT in reference 18

Courtesy of Gwen Chen, Willis-Knighton Cancer Center (WKCC)
Example with brain tumors

- CBCT is best for alignment

More information about CBCT in reference 18

Courtesy of Gwen Chen, Willis-Knighton Cancer Center (WKCC)
Example with Head & Neck

- CBCT is best for alignment

More information about CBCT in reference 18

Courtesy of Gwen Chen, Willis-Knighton Cancer Center (WKCC)
Treatment for moving tumors at TCPT

12% of patients treated with lung cancer

More information about treating lung tumors in reference 18, 19

Courtesy of Andrew Lee, Texas Center for Proton Therapy (TCPT)
TCPT workflow for lung treatment

More information about treating lung tumors in reference 18, 19

Courtesy of Jared Sturgeon, Texas Center for Proton Therapy (TCPT)
Respiratory gating for 4D CT acquisition and gated treatment

More information about treating lung tumors in reference 18, 19

Courtesy of Andrew Lee, Texas Center for Proton Therapy (TCPT)
Improvement of tumor coverage with 4D robust planning

Proton planning with “4D robustness” to improve tumor coverage in all respiratory phases

More information about treating lung tumors in reference 18, 19

Courtesy of Andrew Lee, Texas Center for Proton Therapy (TCPT)
CBCT reconstruction with IBA adaPT software for alignment

More information about treating lung tumors in reference 18, 19

Courtesy of Jared Sturgeon, Texas Center for Proton Therapy (TCPT)
Gating for selected cases with large tumor motion

Gated proton beam during exhale...but actually may prefer beam-on during inhale for lung Ca

UBTI offers opportunity to gate beam or use breath-hold techniques

Lei Dong, PhD

More information about treating lung tumors in reference 18, 19

Courtesy of Andrew Lee, Texas Center for Proton Therapy (TCPT)
Compact solutions makes proton therapy more affordable
The evolution of proton therapy solutions

More information about integration of PT in an existing radiation oncology center in reference 16

Courtesy of Tom Depuydt, ParTICLe proton therapy, UZ Leuven
From a research by-product to an integrated treatment modality

“PT facilities evolves from being …”

A by-product  \[\rightarrow\] Dedicated stand-alone facility  \[\rightarrow\] Embedded Facility

NUCLEAR PHYSICS RESEARCH FACILITY  \[\rightarrow\] PT  \[\rightarrow\] HOSPITAL

Equipment  \[\rightarrow\] Equipment  \[\rightarrow\] Equipment
~100M EUR  \[\rightarrow\] ~60M EUR  \[\rightarrow\] ~25M EUR

PT seen as an additional modality to the armamentarium

More information about integration of PT in an existing radiation oncology center in reference 16

Courtesy of Tom Depuydt, ParTICLE proton therapy, UZ Leuven
Examples of integrated proton therapy solution
Compact system & multi-room system

Compact solution

Typical size: 400 m²

Multi-room solution

Typical size: 2.500 m²
Comparison size with a linac

1 Proteus®ONE vault

27.4m

12.8m

2 linacs’ vault

25.8m

10.9m
Compact solution

- Available from 1 Clinical room up to X Clinical rooms
- Clinical Focus: PBS, CBCT, IGRT
- If installed in an existing RT Center, a dedicated CT, MRI or PET CT is not necessary
- ...the same goes for OIS and TPS systems
- Can treat from 300 up to 500 patients per year
- Project Time overall: 36 to 48 months
- Equipment price ~25M EUR

Multi-room solution

- Available from 1 Clinical room up to 5 Clinical rooms
- Typical Proton Therapy project is for 3 rooms
- Customized design: PBS, Double Scattering, Fixed beam and/or research line
- Dedicated CT, MRI or PET CT
- Dedicated OIS and TPS systems
- Can treat up to 1,300 patients per year (3 rooms)
- Project Time overall: 48 months
- Equipment price ~60M EUR

Designed to be integrated in an existing RT center

PT seen as an additional modality to the armamentarium
Advantages of an integrated compact PT solution

- Compact PT systems will facilitate embedding of PT facilities in an existing hospital campus
- Embedded facilities have an impact on the organization of PT:
  - Located in close proximity/adjacent to existing general hospital/existing RT service
  - Allow better integration in existing RT organization, in all aspects
  - Potentially will amplify the interaction/crosstalk between PT and conventional RT/XT
  - This integration can play a role in coming to optimal choice of treatment modality, PT vs XT

More information about integration of PT in an existing radiation oncology center in reference 16

Courtesy of Tom Depuydt, ParTICLE proton therapy, UZ Leuven
Up to 30 patients can be treated per day in an extended shift.
Clinical PT smart workflow for higher throughput

1. Open environment to ease patient setup
2. Ambient experience to decrease patient anxiety
3. Wireless hand pendant to increase staff comfort
4. Unique instantaneous imaging available all the time
5. Remote operation of accessories

More information about Proteus®ONE workflow in reference 20, 21
Treatment of large range of indications

First 500 patients treated at Willis-Knighton, LA, US

- Lung: 43%
- Gastrointestinal: 15%
- Gynecological: 10%
- Breast: 9%
- Prostate: 7%
- Brain: 5%
- Head & Neck: 4%
- Others: 6%
- Others: 10%
Today at Willis-Knighton

16 Mean treatment time per patients

Up to 30 fractions per day in 9-10 hours

98.24% Average uptime in 2018 (up to August 2018)
Generation of clinical evidence is moving forward. Be active and participate in clinical trials
Increasing acceptance of proton therapy benefits

Number of centers increases

Number of patients increases

Number of trials/data increases

Number of publications increases

Number of guidelines increases

18 additional rooms in 2017

23,000* additional patients in 2017

160** open trials in 2017

629** publications in 2017

ASTRO & NCCN guidelines update in 2017

More patients

*IBA internal modeling based on PTCOG reports

**More information about clinical trials in reference 7 and clinical papers in reference 1
Recognition of the clinical advantages of proton therapy

629
Scientific articles published in 2017

160
Trials ongoing as of the end of 2017

Types of cancer for which clinical trials using proton therapy treatment are being conducted

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- Brain / Central Nervous System / Base of skull: 24%
- Pediatric: 23%
- Eye: 4%
- Prostate: 21%
- Lung: 16%

More information about clinical trials in reference 7 and clinical papers in reference 1
Multi-centers initiatives to gather compelling clinical evidence

- Multi-institutional proton therapy patient registry with over 10,000 patients from 12 facilities in the US
- International data steering committee
- High quality data with advanced dosimetry and imaging data
- Quicker and more robust data collection

- Build European-wide integrated platform to collect clinical information including imaging and develop standards of care in RT
- Enhance evidence-based particle therapy
- Co-led by EORTC and EPTN (European Proton Therapy Network) now part of ESTRO
- Model-based approach as an alternative to RCT's
- Start a prospective PT registry including all PT patients in Europe
- Expected to be running in 1 year and recruit 2000 patients in 5 years

More information about PCG in reference 10, and EPTN/EORTC in reference 11, 12, 13
Installation time has never been so fast
Typical equipment installation time

Building construction:
- Building occupancy date (BOD)
- Building support with our partners
- Rigging
- Beam production system

Equipment installation:
- 12 months
- Beam calibration
- Beam safety and performances
- Position management system
- System validation
- Customer acceptance
- System delivery
- Clinical commissioning
- 1st patient
Compact solutions setting the new standard in installation

Samples of the last 5 Proteus®ONE equipment installations*

Proteus®ONE (2018)
Rutherford CC, Newport, UK
9 months**

Proteus®ONE (2018)
Hokkaido Ohno, Sapporo, Japan
11 months

Proteus®ONE (2017)
Beaumont, Royal Oak, USA
12 months

Proteus®ONE (2018)
Toyohashi, Japan
10 months**

Proteus®ONE (2018)
Cyclhad/Archade, Caen, France
12 months

* From rigging to acceptance  ** Non standard installation
List of reference


## List of proton therapy centers – part 1

<table>
<thead>
<tr>
<th>List of proton therapy centers</th>
<th>Year of sales</th>
<th>Vendor</th>
<th>No of Rooms</th>
<th>Country</th>
<th>3 Regions</th>
<th>Treating</th>
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<tbody>
<tr>
<td>Tokushukai Medical Group</td>
<td>2018</td>
<td>Hitachi</td>
<td>1</td>
<td>Japan</td>
<td>Asia</td>
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<tr>
<td>Jiangxi Cancer Hospital</td>
<td>2018</td>
<td>Mevion</td>
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<td>China</td>
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<td>University of Miami</td>
<td>2017</td>
<td>Varian</td>
<td>1</td>
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<td>Europe and ROW</td>
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