






Health Economics and perspective in particle therapy

ENLIGHT meeting, Utrecht, 16 September 2016

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CZ-group is third largest Dutch health insurer



| | |
|------------------------|---|
| Number of insured: | 3.4 million |
| Market share: | 20% |
| 3 Labels: |    |
| Insurance premium: | € 8.4 billion |
| Operating costs: | € 324 million |
| As % of premium: | 3.9 % |
| Solvability %: | 286 % |
| Employees: | 2.600 |
| Customer satisfaction: | 7.9 |

Content

Background economics

Cost-effectiveness protons

Patient selection

Proton therapy in the Netherlands

Summary and discussion

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Because of significant growth in Health Care Cost, Health Economics are gaining more importance

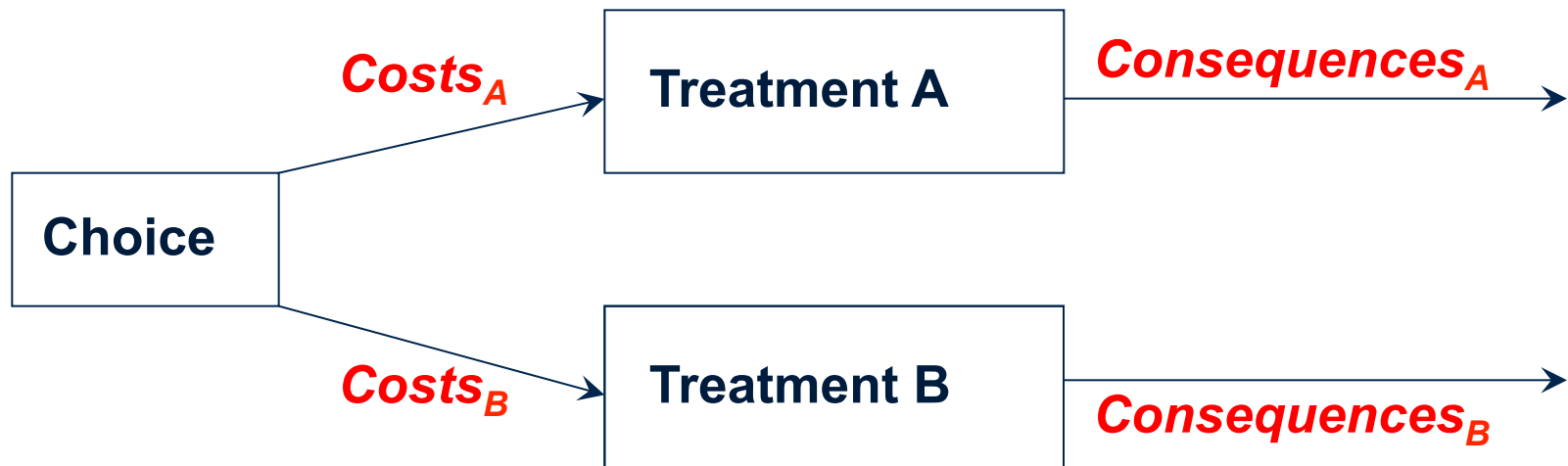


% gross domestic product (GDP)

spending in € per person

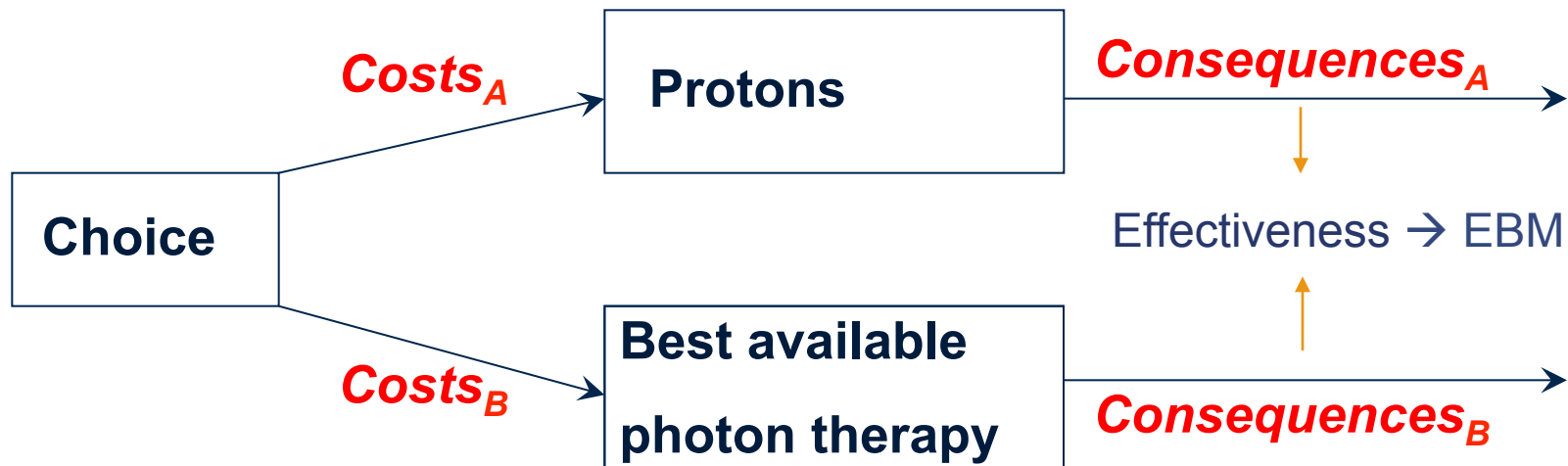
Cost-effectiveness analysis

= The comparative analysis of alternative courses of action in both their costs and consequences



Cost-effectiveness analysis

Medical Economics seeks evidence to provide evidence for the utilization of up-and-coming technologies so as to provide economic sustainability



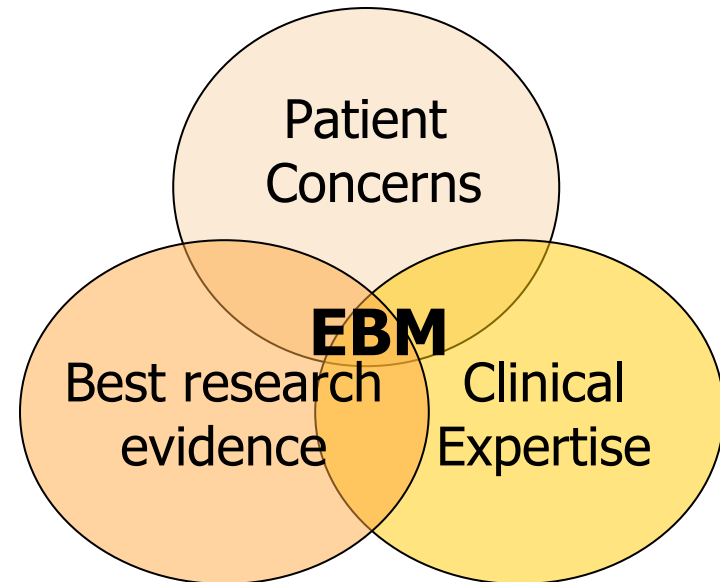
What is Evidence Based Medicine?

The integration of:

- Best Research Evidence with
- Clinical Expertise and
- Patient Values

Goal:

- Improve outcomes
- Improve quality of care
- Provide standardization



Several systems to assess the quality of evidence

Centre for Evidence-Based Medicine, Oxford (1a-5)

SORT: Strength-of-Recommendation Taxonomy (A,B,C)

Practice Guidelines rating scales (various)

GRADE: Grading of Recommendations Assessment, Development and Evaluation (A,B,C,D)

| Medscape® www.medscape.com | | |
|--|---|-------------------------|
| Level of Evidence | Grading Criteria | Grade of Recommendation |
| 1a | Systematic review of RCTs including meta-analysis | A |
| 1b | Individual RCT with narrow confidence interval | A |
| 1c | All and none studies | B |
| 2a | Systematic review of cohort studies | B |
| 2b | Individual cohort study and low quality RCT | B |
| 2c | Outcome research study | C |
| 3a | Systematic review of case-control studies | C |
| 3b | Individual case-control study | C |
| 4 | Case-series, poor quality cohort and case-control studies | C |
| 5 | Expert opinion | D |

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Trade-off

A new treatment/technology is considered to be accepted as compared to standard treatment if:

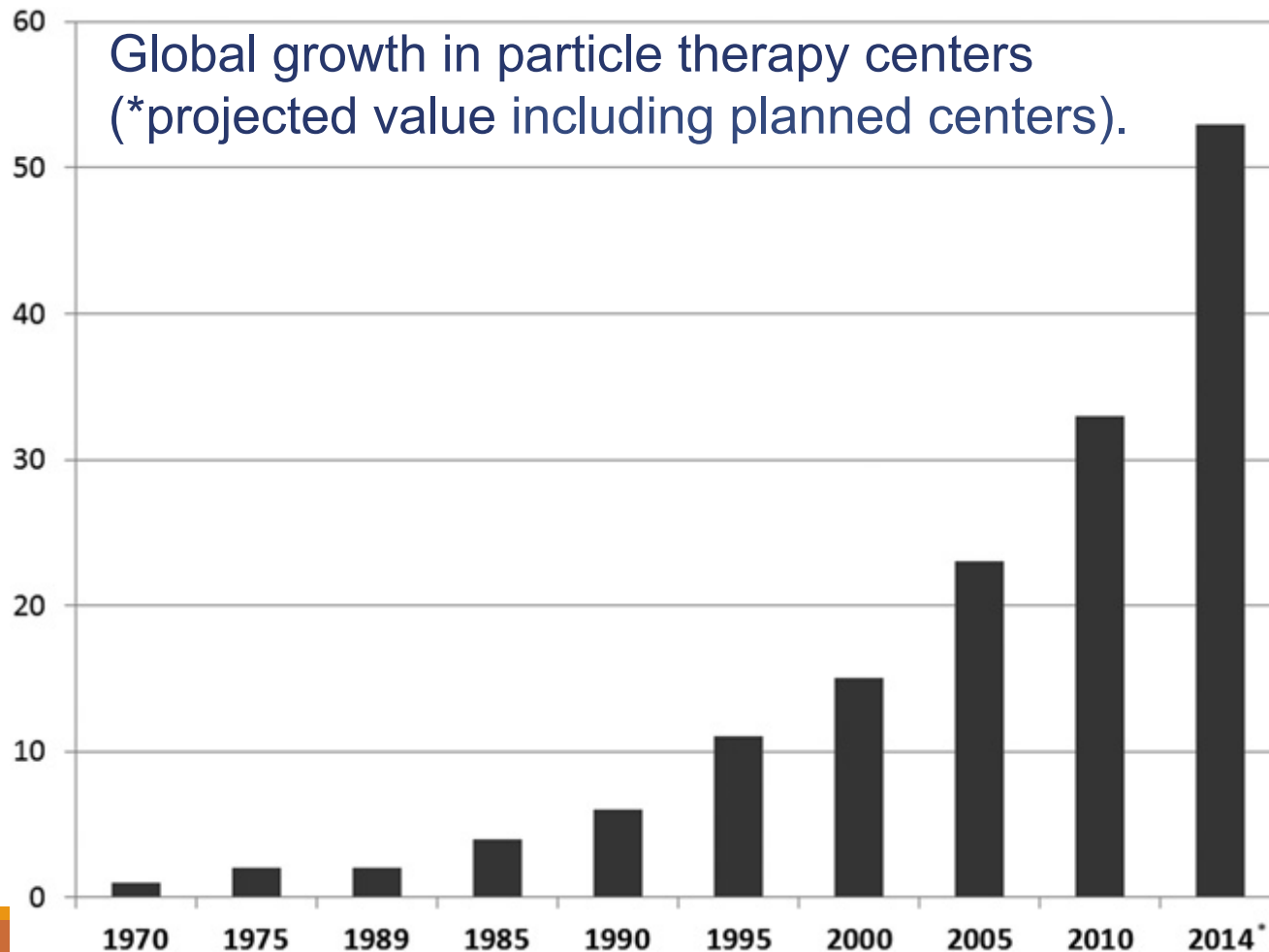
- Better survival rates
- and/or a better QoL
- Acceptable costs

Limited CEAs for protons for different indications

| | Tumor site | Design | Outcome | Result | Report uncertainty |
|-----------------|---------------------|------------------------|---------|----------|--------------------|
| Lundkvist, 2005 | Breast | Markov | QALY | €10.130 | no |
| Lundkvist, 2005 | Medulloblastoma H&N | Markov | QALY | €10.130 | no |
| Lundkvist, 2005 | Prostate | Markov | QALY | - | no |
| Jakel, 2007 | Prostate | Retrospective analysis | LYG | € 7.692 | no |
| Konski, 2007 | Prostate | Markov | QALY | \$63,578 | no |
| Grutters, 2010 | NSCL | Markov | QALY | €67,257 | yes |
| Maboraki, 2010 | Rectum | Retrospective analysis | LYG | - | no |

high level of uncertainty: many assumptions, suboptimal methodology

However, number of proton facilities are growing,
based on the theoretical advantage and.....
clinical expertise



2016: Highly unlikely that PBT will be the most economic options for all cancers or even for all patients with a given type of cancer

- Lack of evidence (mainly due to lack of comparable data)
- sub-optimal methodology CEA, also not comparable
- Patient selection needed

Verma V, Mishra MV, Mehta MP. A systematic review of the cost and cost-effectiveness studies of proton radiotherapy. Cancer. 2016 May 15;122(10):1483-501.

Verma V, Shah C, Rwigema JC, Solberg T, Zhu X, Simone CB 2nd. Cost-comparativeness of proton versus photon therapy. Chin Clin Oncol. 2016 Aug;5(4):56.

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Patient selection by combining in silico data with NTCP

International Journal of
Radiation Oncology
biology • physics

www.redjournal.org

Volume 85 Number 5 2013

Clinical Investigation

Protons in Head-and-Neck Cancer: Bridging the Gap of Evidence

Bram L.T. Ramaekers, MSc,^{*,†} Janneke P.C. Grutters, PhD,^{*}
Madelon Pijls-Johannesma, PhD,[†] Philippe Lambin, PhD,[†] Manuela A. Joore, PhD,^{*,†}
and Johannes A. Langendijk, PhD[§]

Aim: Given the lack of data, estimate the cost-effectiveness of protons in H&N cancer (IMRT vs IMPT)

Main endpoint: xerostomia and/or dysphagia

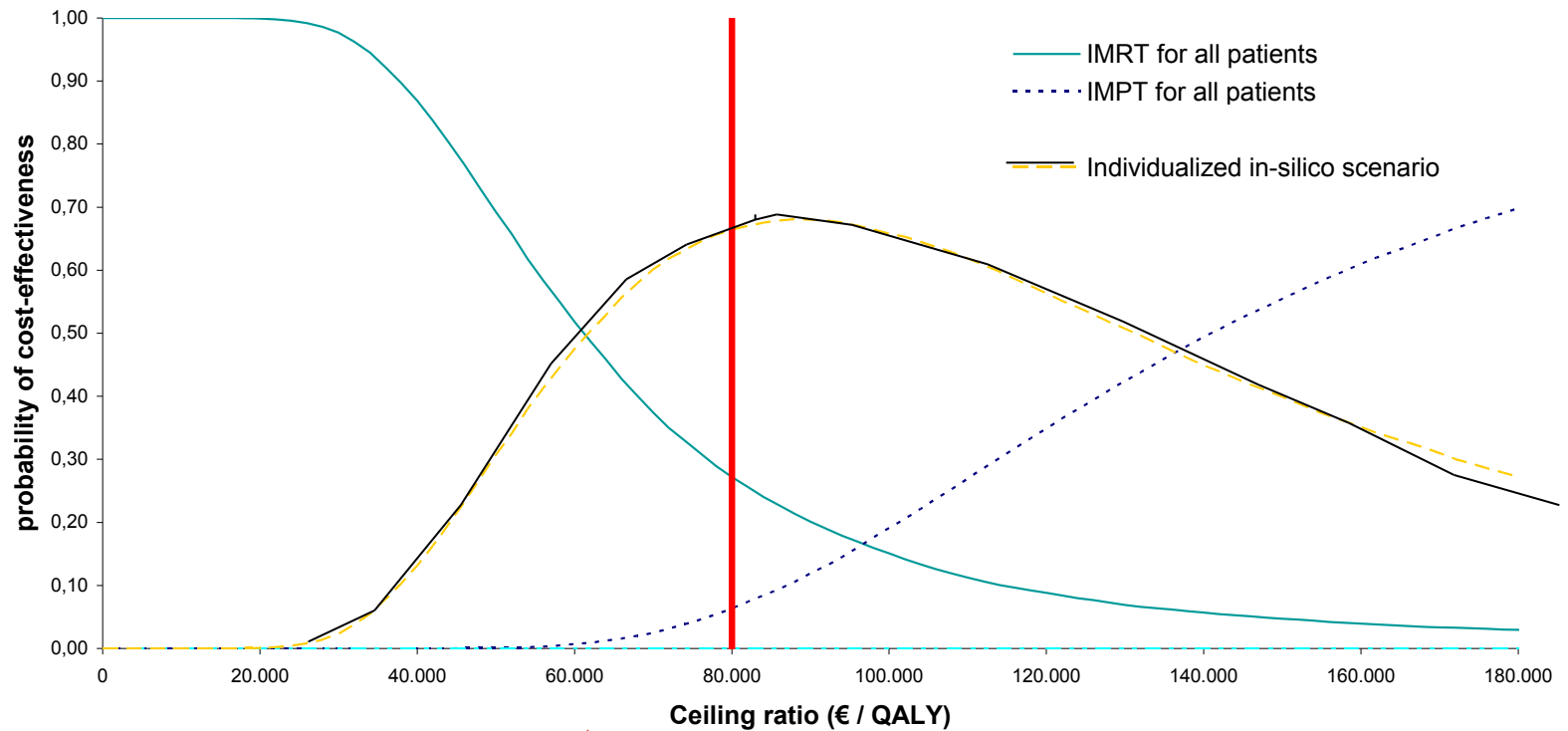
- according to available NTCP models*
- dose parameters were derived from in silico trials

* Beetz et al. Radioth Oncol 2010;96:S84-S85.

Christianen et al. Radiother Oncol 2012;105:107-114.

IMPT in H&N cancer cost-effective for subgroup of patients

Cost-effectiveness Acceptability Curves

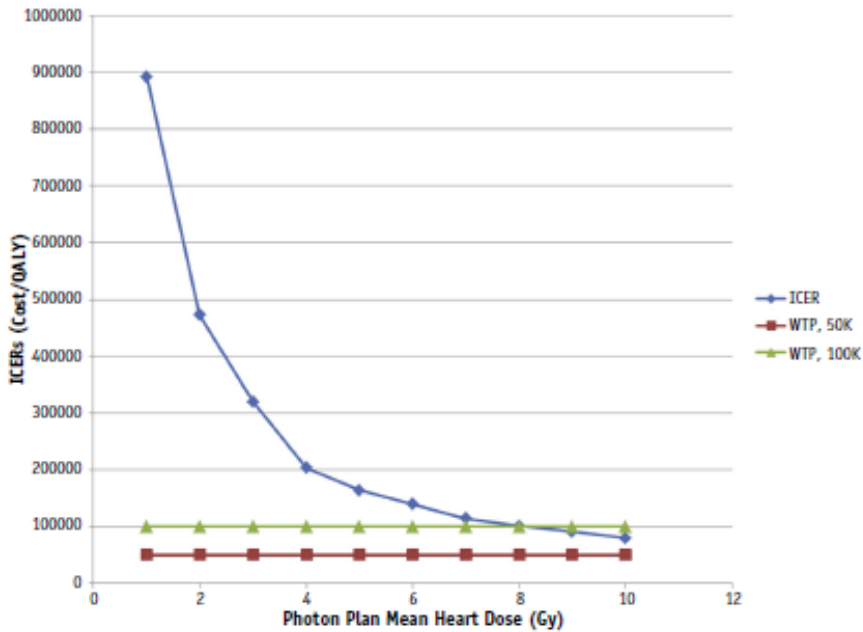


Will patient selection contribute to cost-effectiveness of protons in breast cancer treatment?

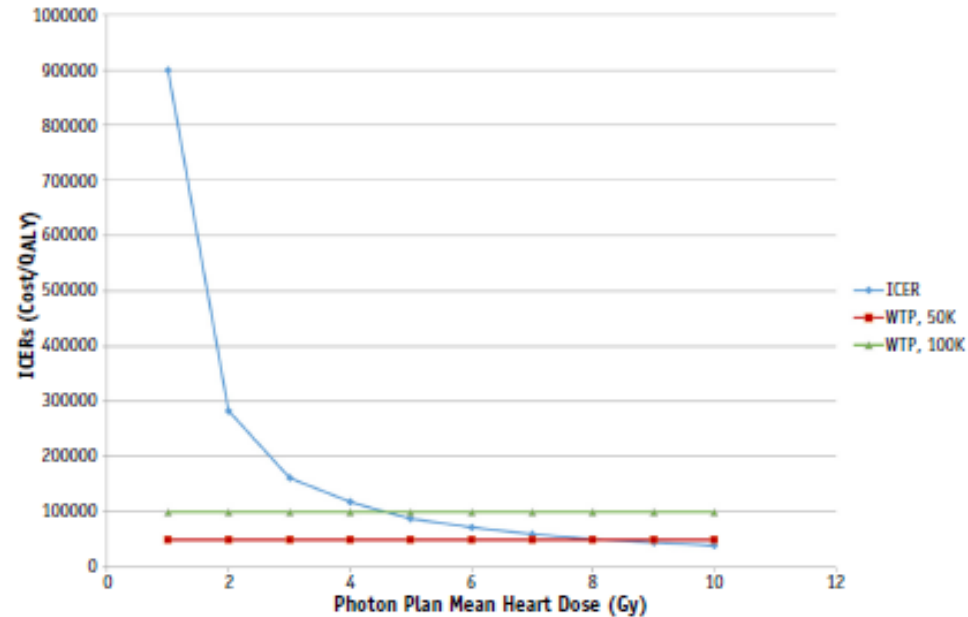
- CEA, Markov model
- photon versus protons
- different strata based on age (40y,50y,60y) and presence/lack of cardiac risk factors (CRF)

Protons for breast-cancer only cost-effective if ≥ 1 CRF and MHD ≥ 5 Gy

ICERS between Photon and Proton RT per Gy of MHD for 50yoF with no cardiac RF



ICERS between Photon and Proton RT per Gy of MHD for 50yoF with at least one cardiac RF



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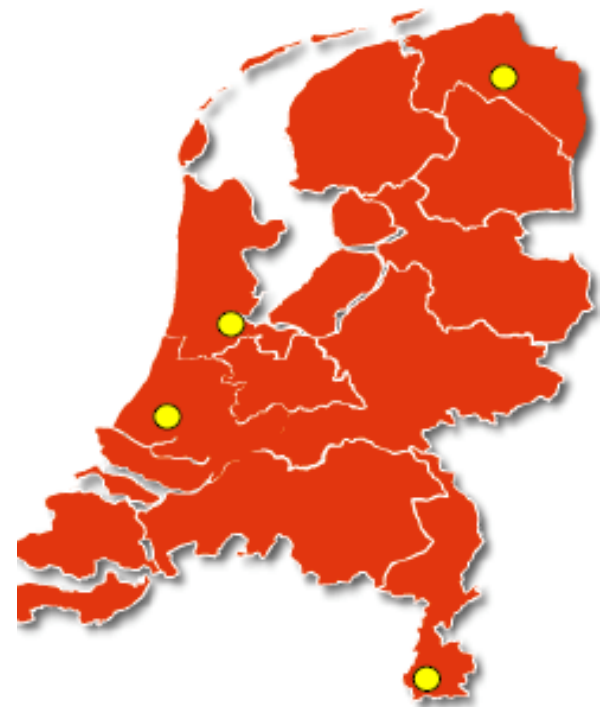
Summary and discussion

Proton therapy in The Netherlands

Maximum of 4 facilities are granted

Treatment capacity of 2200 patients/year

- Amsterdam: 600 pat/yr
- Groningen: 600 pat/yr
- R'dam/Delft/Leiden: 600 pat/yr
- Maastricht: 400 pat/yr



Model based approach is adopted by the Health Council

NTCP models will be used to select patients who are likely to benefit from proton therapy (prevention of side effects)?

Radiotherapy and Oncology 107 (2013) 267–273



Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

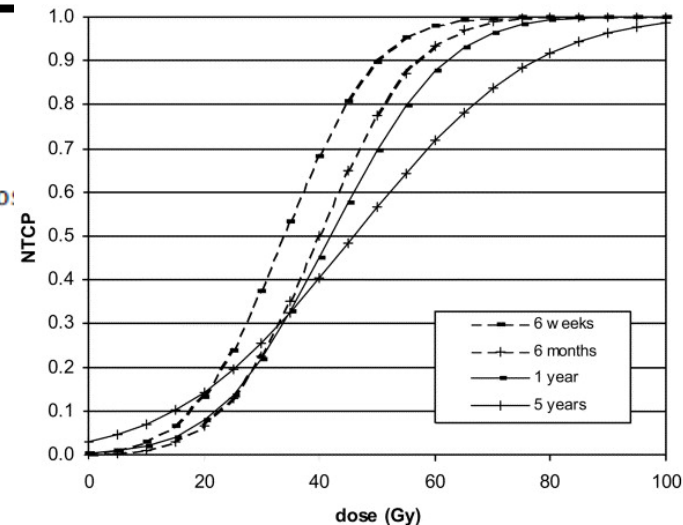
journal homepage: www.thegreenjournal.com



Proton radiotherapy

Selection of patients for radiotherapy with protons aiming at reduction of side effects: The model-based approach

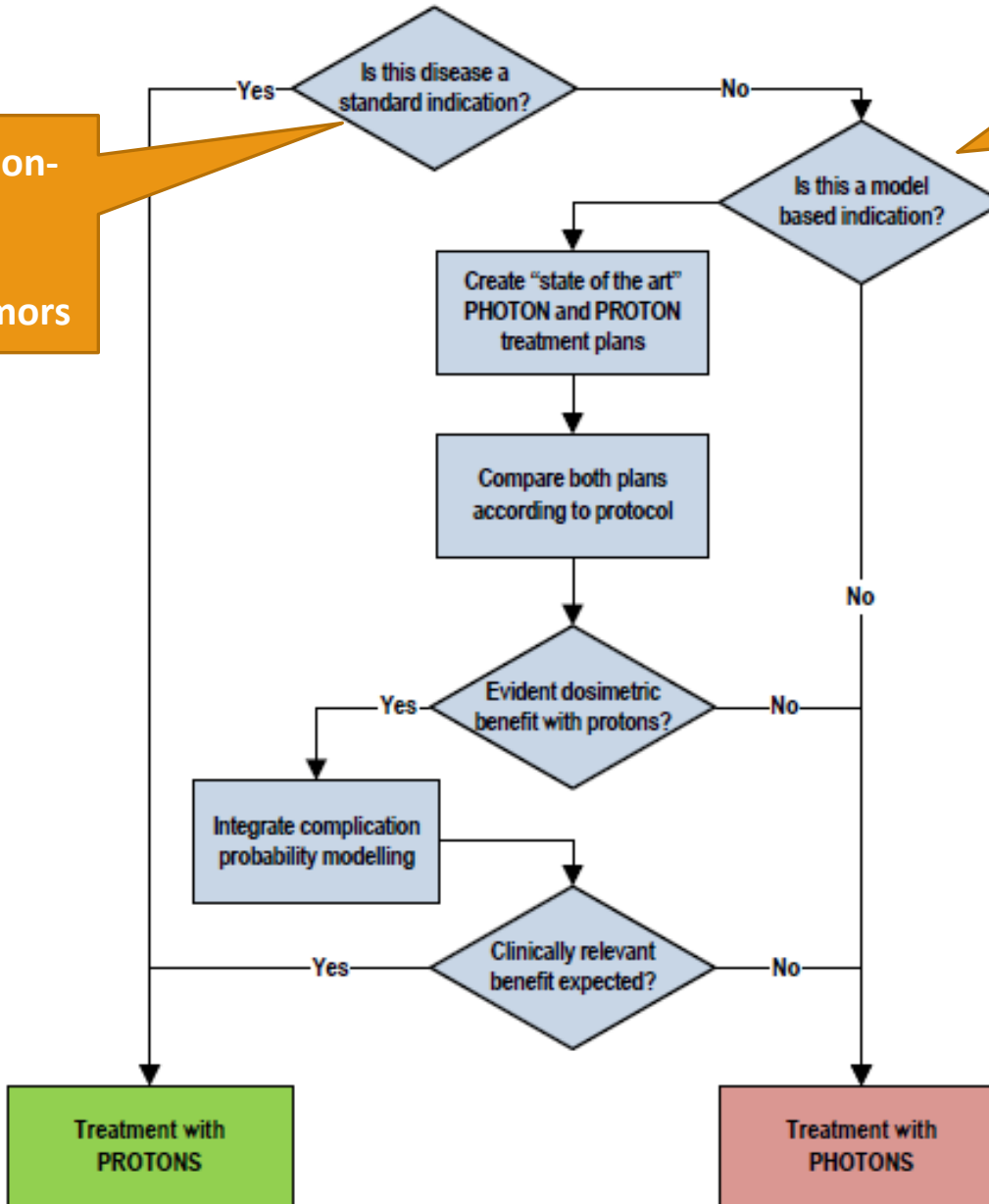
Johannes A. Langendijk^{a,*}, Philippe Lambin^b, Dirk De Ruyscher^c, Joachim Widder^a, Mike Bo: Marcel Verheij^e



price agreements made for first 3 years

- Different prices per proton center
- price based on expected number of patients/year
- if less patients will be referred, price per patient will increase
- also start-up costs can be integrated in the price

Proton therapy reimbursement decision tree for the Netherlands



- Chordomas/chondrosarcomas
- Pediatrics
- Intraocular tumors

- Breast
- Lung
- Head&Neck
- Prostate

Decision support systems will play an important role in patient selection

PredictCancer.org
CANCER PREDICTION MODELS

Home Predict Cancer app Models Publish models News Links Contact Legal

Cost-effectiveness of IMPT versus IMRT for head and neck cancer*

Input parameters

Treatment independent parameters

Willingness to pay (€) per QALY gained:

€

| Treatment dependent dose parameters | IMRT | IMPT |
|--|----------------------|----------------------|
| Mean dose to the ipsilateral parotis (Gy) | <input type="text"/> | <input type="text"/> |
| Mean dose to the contralateral parotis (Gy) | <input type="text"/> | <input type="text"/> |
| Mean dose to the pharyngeal constrictor muscle superior (Gy) | <input type="text"/> | <input type="text"/> |
| Mean dose to the supraglottic area (Gy) | <input type="text"/> | <input type="text"/> |

Radiotherapy and Oncology 118 (2016) 281–285



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journal homepage: www.thegreenjournal.com



Particle therapy in head and neck cancer

Development and evaluation of an online three-level proton vs photon decision support prototype for head and neck cancer – Comparison of dose, toxicity and cost-effectiveness



Qing Cheng^{a,1}, Erik Roelofs^{a,1}, Bram L.T. Ramaekers^b, Daniëlle Eekers^a, Johan van Soest^a, Tim Lustberg^a, Tim Hendriks^a, Frank Hoebbers^a, Hans Paul van der Laan^c, Erik W. Korevaar^c, Andre Dekker^a, Johannes A. Langendijk^c, Philippe Lambin^{a,*}

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Summary

- It seems hard, or even impossible, to estimate the cost-effectiveness of proton therapy based on the published literature.
- A model-based approach could be the solution based on subgroup or individual patients.
- Modeling should complement clinical trials, not replace (RCTs remain the ideal tool for research in proton radiotherapy)
- Next, it is possible to assess the effectiveness of proton therapy for individual patients, comparing photon and proton treatments on dose metric, toxicity and cost-effectiveness levels, retrieved from a decision support system.
- Individualized patient selection will enhance the cost-effectiveness of proton therapy (www.predictcancer.org)
- Patient values should be taken into account

Discussion

- How to standardize and control patient selection?
- Will 2200 patients be referred in The Netherlands, since at current (2016) < 50 patients/year are referred to proton centers abroad?
- So, are we creating overcapacity in The Netherlands?
- What financial consequences will 4 PT centers have for the RT departments /hospitals with only photon therapy?
- Will we succeed to increase value in health care by the introduction of protons in The Netherlands? How can this be measured?

Thank for your attention!

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