Figure S1. Minimum number of treatment beam orientations for different treatment sites (22 centres answered).
Table S1.
Number of proton therapy centres applying a restriction on the minimum number of beam orientations for different treatment sites.

<table>
<thead>
<tr>
<th>Treatment site</th>
<th>Minimum number of beam orientations</th>
<th>Rarely/not treated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
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<tr>
<td>Base of skull</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>Brain</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Breast</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Craniospinal irradiations</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Head &amp; neck</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Liver</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Lung</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Prostate</td>
<td>0</td>
<td>10</td>
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## Participating centres

<table>
<thead>
<tr>
<th>Country</th>
<th>City</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>Wiener Neustadt</td>
<td>MedAustron Ion Therapy Centre</td>
</tr>
<tr>
<td>Belgium</td>
<td>Leuven</td>
<td>Particle, UZ Leuven</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>Prague</td>
<td>PTC Czech</td>
</tr>
<tr>
<td>Denmark</td>
<td>Aarhus</td>
<td>Aarhus University Hospital</td>
</tr>
<tr>
<td>France</td>
<td>Caen</td>
<td>Centre François Baclesse</td>
</tr>
<tr>
<td>France</td>
<td>Nice</td>
<td>Centre Antoine-Lacassagne</td>
</tr>
<tr>
<td>France</td>
<td>Paris</td>
<td>Institut Curie</td>
</tr>
<tr>
<td>Germany</td>
<td>Berlin</td>
<td>Charité - universitätsmedizin Berlin</td>
</tr>
<tr>
<td>Germany</td>
<td>Dresden</td>
<td>OncoRay</td>
</tr>
<tr>
<td>Germany</td>
<td>Essen</td>
<td>WPE gGmbH</td>
</tr>
<tr>
<td>Germany</td>
<td>Heidelberg</td>
<td>Heidelberg Ion Beam Therapy Center (HIT)</td>
</tr>
<tr>
<td>Germany</td>
<td>Marburg</td>
<td>Marburger Ionenstrahl-Therapiezentrum</td>
</tr>
<tr>
<td>Italy</td>
<td>Catania</td>
<td>NFN-LNS</td>
</tr>
<tr>
<td>Italy</td>
<td>Pavia</td>
<td>CNAO National Institute for Oncological Hadrontherapy</td>
</tr>
<tr>
<td>Italy</td>
<td>Trento</td>
<td>APSS</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>Delft and Rotterdam</td>
<td>Holland Proton Therapy Center and Erasmus University Medical Center</td>
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<td>University Medical Center Groningen</td>
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<td>Maastricht</td>
<td>Maastro Clinic</td>
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<td>Krakow</td>
<td>Institute of Nuclear Physics PAN - Cyclotron Centre Bronowice</td>
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<tr>
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<td>Madrid</td>
<td>Clínica Universidad de Navarra</td>
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<td>Spain</td>
<td>Pozuelo de Alarcon</td>
<td>Centro de Protonterapia Quironsalud</td>
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<tr>
<td>Sweden</td>
<td>Uppsala</td>
<td>The Skandion Clinic</td>
</tr>
<tr>
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<td>Villingen</td>
<td>Paul Scherrer Institute</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>Manchester</td>
<td>The Christie Proton Therapy Centre</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>Newport</td>
<td>Rutherford Cancer Centres</td>
</tr>
</tbody>
</table>
Contact Details

Please fill out all fields below (mandatory fields are marked with a *)

* 1. What is your last name?

* 2. What is your e-mail address

* 3. What is the name of your institution?

* 4. In which city is your institution located?

* 5. In which country is your institution located?
1. What is the minimum number of beam orientations you use in a proton therapy plan?
   - 1
   - 2
   - 3
   - 4
   - 5
   - more
   - Other (please specify)

2. Does the minimum number of beam orientations differ for different treatment sites?
   - Yes
   - No
**ESTRO (EPTN-WP6): RBE considerations in proton therapy**

**Number of fields**

**Different treatment sites**

1. What is the minimum number of treatment beam orientations?

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>more</th>
<th>rarely treated</th>
<th>not treated</th>
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<tbody>
<tr>
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<td></td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td>Brain</td>
<td></td>
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</tr>
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<tr>
<td>Craniospinal irradiation</td>
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<td>Liver</td>
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<td>Lung</td>
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<td>Pancreas</td>
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<td>Prostate</td>
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</tr>
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<td></td>
</tr>
</tbody>
</table>

(continued on page 4)
Beam angle selection

1. Do you apply restrictions on angles between proton beams?
   - No
   - Yes
   - Other (please specify)

2. Which restrictions do you apply on beam angles?

3. For which tumor entities do you apply restrictions on beam angles?

Field weights

4. Do you apply constraints regarding the relative field weights?
   - No constraints apply.
   - All fields should have comparable relative weight.
   - The following constraints apply for the relative field weight:
Beam stopping

1. Do you avoid field configurations where a beam stops in front of or inside an organ at risk (OAR)?
   - [ ] Yes
   - [ ] No
   - [ ] Other (please specify)

2. How do you avoid beams stopping in an OAR? [multiple answers possible]
   - [ ] Field angles are avoided that result in beams stopping in an OAR.
   - [ ] Fields stopping in or close to an OAR have a low weight.
   - [ ] Field ranges are extended to place the end of range beyond an organ at risk (“shoot-through”).
   - [ ] Other:
     Please specify your strategy
Robust optimization

1. Do you apply robust optimization for dose planning?
   - Yes
   - No
   - Other (please specify)

2. What is considered for robustness in the optimization?
   - Target coverage.
   - Dose constraints for selected OAR and target coverage.
   - Dose constraints for all OAR and target coverage.
   - Dose constraints for OAR.
   - Other (please specify)
Variability of RBE in treatment planning (I/II)

Active consideration of variable RBE

1. Do you consider the possibility during clinical treatment planning or plan approval that the proton RBE may be variable?
   - No, never.
   - In some cases.
   - Regularly.
   - Always.
   - Other (please specify)

2. When do you actively consider the possibility of a variable proton RBE? [multiple answers possible]
   - Individual decision.
   - For specific beam arrangements/treatment plans.
   - For specific patient groups.
   - For specific tumor sites.
   - Never.
   - Other (please specify)

3. Where do you actively consider the possibility of a variable RBE? [multiple answers possible]
   - Organs at risk.
   - Target volume.
   - Organs at risk and target volume.
   - Nowhere.
   - Other (please specify)
4. What kind of measures do you apply to consider/counteract a potentially variable proton RBE? [multiple answers possible]

- Take special care about beam arrangements.
- Avoid proton beams to stop in or adjacent to organs at risk.
- Perform robust optimization.
- Consider the LET distribution for a treatment plan.
- Consider a variable RBE distribution for a treatment plan.
- Use LET or RBE for treatment plan optimization.
- Nothing.
- Other measures (please specify)
Variability of RBE in treatment planning (II/II)

**Prescription of a variable RBE**

1. Do you prescribe anything else than a fixed RBE of 1.1 for patient treatment?
   - Yes
   - No

2. In which cases do you apply an RBE concept different from RBE = 1.1? [multiple answers possible]
   - Never.
   - Individual decision.
   - For specific beam arrangements/treatment plans.
   - For specific patient groups.
   - For specific tumor sites.
   - Within a clinical study on RBE.
   - Always.
   - Other (please specify)

3. If applicable: Please provide a short description of your RBE concept.
Frequency of LET or RBE calculation

1. Do you perform any patient-specific LET or RBE calculations to support treatment planning?
   - Yes
   - No

2. What is the frequency for performing patient-specific LET or RBE calculations?
   - Never.
   - Occasionally.
   - Regularly.
   - Always.
   - Other (please specify)

3. If applicable: What is triggering the calculation of LET or RBE?

Clinical workflow

4. Which quantities do you calculate for clinical treatments? [multiple answers possible]
   - LET distribution.
   - RBE distribution.
   - Track-end distribution.
   - Biological effect.
   - NTCP with variable RBE.
   - None of these.
   - Other quantities (please specify)
Clinical workflow

1. How do results of these calculations enter clinical practice? [multiple answers possible]
   - Never used.
   - During the treatment planning process.
   - For plan evaluation or plan approval.
   - In the course of robust optimization.
   - For documentation.
   - For retrospective analysis to support patient follow-up.
   - For clinical research purposes.
   - Other (please specify)

2. Who initiates the calculation of LET or RBE in clinical praxis? [multiple answers possible]
   - Treating physician.
   - Physicist.
   - Dosimetrist.
   - Standard procedure.
   - Never performed.
   - Other (please specify)

3. Who performs the calculation of LET or RBE in clinical praxis? [multiple answers possible]
   - Treating physician.
   - Physicist.
   - Dosimetrist.
   - Research staff.
   - Never performed.
   - Other (please specify)
Specification of LET or RBE calculation

1. If applicable: Please specify the software you use to perform these calculations.

2. If applicable: Please specify the tumor entities for which you perform these calculations.

3. If applicable: Please provide additional specification to better characterize the calculations.
RBE consideration for patient follow-up

Consideration of RBE in follow-up

1. Do you consider RBE in any way during patient follow-up? [multiple answers possible]
   - No.
   - Yes, in an attempt to better understand individual radiation response.
   - Yes, within a (retrospective) study to estimate clinical RBE data.
   - Yes, but in another way. (please specify)

2. If applicable: How do you consider RBE in follow-up?

3. If applicable: For which tumor sites do you consider RBE in follow-up?

Implementation of other RBE measures

4. Have you implemented any other measure at your clinic in connection with RBE which has not been considered in this questionnaire?
Your wish list concerning proton RBE

1. What would you like to change in your treatment workflow with respect to RBE?

2. What kind of evidence should be generated to consider variable proton RBE in patient treatment?

3. What kind of treatment planning tools should be developed by vendors to consider variable proton RBE in patient treatment?

4. Which kind of guidelines do you miss in the context of a variable proton RBE?

5. What kind of publications are you missing?

6. What else are you missing or wish to see in the future concerning the proton RBE?
1. Add any additional comments below

Thank you very much for your kind participation!

Your valuable contribution is highly appreciated.