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Highlights

- Barriers for access to proton therapy were unraveled in a mixed-methods study
- Methods consisted of a survey, interviews and workshops with direct stakeholders
- Main barriers were referral logistics, multi-disciplinarity, methods for selection
- To improve access it is important to investigate issues in the patient-journey
- After joining forces with referrers, promising interventions were designed

Acknowledgements

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Abstract

Background and purpose

The Netherlands has National Indication Protocols on proton therapy (PT) to select patients who benefit most from PT. However, referrals to proton therapy centres (PTCs) are lagging. The objective
of this research is to identify the barriers for access to PT and to design interventions to address these barriers. Material and methods

We conducted a nationwide survey among radiation oncologists (ROs), and semi-structured in-depth interviews with ROs and patients. Subsequently, four workshops were held, in which ROs from one PTC and ROs from referring hospitals participated. The workshops were based on design-thinking research, where ideas were co-created on a multidisciplinary basis to encourage joint problem ownership. Kruskal Wallis and X2 tests were used to analyze data.

Results

The most prominent barriers mentioned by ROs were patient selection, poor logistics, and logistical worries about the combination of radiation treatment with chemotherapy. Patients pointed out the inefficient coordination between organisations, poor communication, travel issues and discomfort during treatment. Clues to increase referrals revealed the need for additional tools for patient selection and innovative ways to improve logistics. A case manager was identified as beneficial to the patients’ journey as part of a multidisciplinary approach. Such an approach should include the active involvement of medical oncologists, surgeons and pulmonologists.

Conclusion

Barriers for access to PT were identified and prioritized in the inter-organisational care-pathway of proton therapy patients in The Netherlands. Innovative solutions were co-designed to solve the barriers.

Introduction

Due to the physical properties of protons, proton therapy (PT) offers the potential to reduce dose to organs at risk, and thereby side effects of radiation treatment (e.g. heart damage, swallowing problems, cognition loss). A reduction in side-effects is expected to improve quality of life (1) and possibly even survival, since survival has been shown to be related to the dose to the heart (1–3). However, as the costs of PT are almost two-and-a-half times higher than conventional therapy, it is essential to select patients that would benefit the most (4,5). When patients are carefully selected, the high costs of PT are expected to be balanced by the lower costs required to cope with fewer and less serious adverse effects (6,7). In the Netherlands, it was decided that a model-based approach would be recognised as a valid selection tool. However, this is dependent on a national indication protocol for PT (NIPP) being approved for that specific indication by the Dutch Health Care Institute. The NIPP should contain validated prognostic models, where the probability of side effects can be calculated (4,5). For PT to be reimbursed, a planning comparison must be carried out on the estimated difference in risk in side effects between PT and photon therapy, for an individual RT treatment plan. This must exceed a specific threshold, as defined by the Dutch Society for Radiation Therapy and Oncology (Nederlandse Vereniging voor Radiotherapie en Oncologie – NVRO). Since January 2018, three proton therapy centres (PTCs) have opened their doors in the Netherlands: 1) University Medical Centre Groningen PTC, 2) Holland PTC (Delft) and 3) Maastro (Maastricht).

Even though the NIPPs have been approved by the NVRO, major adoption challenges for radical innovations, such as PT, remain. In the forecasts, it was estimated that the three centres would collectively treat 1,600 patients with PT in 2020 (8). In addition, around 5,800 patients (11.6% of all radiotherapy patients in the Netherlands) would have the potential to be eligible for PT (8). However, from January 2018 up to 1 July 2022, only 2,897 patients had been treated with PT in The Netherlands. Although the numbers of patients treated are increasing steadily, the 1,600 patients per year estimate has not yet been reached, which cannot be entirely explained by the COVID-19 pandemic. Until now, most patients (76%) receiving PT were referred by the RT department of the PTC itself, indicating that
the opportunity to be treated with PT was much lower for patients originating from RT departments without PT (Table 1) (9).

Implementation and adoption problems for PT were extensively and qualitatively described in a recent publication (10). The primary aim of the current study is to identify barriers for access to PT and to design interventions to address these barriers.

**Materials and methods**

The design is a mixed-methods study consisting of a nationwide survey combined with in-depth interviews and workshops to get a deeper understanding of the barriers. We set up a nationwide survey amongst radiation oncologists (ROs), Ros in training and physician assistants (n=330) to get a general impression of barriers and clues for intervention. Subsequently we interviewed ROs (n=10) and patients (n=7) to discuss the results of the survey in order to prepare the content of the workshops. Participants were limited to referring ROs from lung and oesophageal cancer (care-paths with many barriers) from the four referring hospitals to one of the PTCs and ROs from that PTC (n=17).

(Figure 1).

The survey was developed according to the Consolidated Framework for Implementation Research (CFIR). This is a universally used, well operationalised, multilevel implementation determinant framework, including 39 constructs arranged across five domains. The CFIR points out factors found to influence implementation outcomes and was therefore a useful guide to structure the survey scientifically (11–13). The survey contained multiple choice, open-ended or 5-point Likert scale (1 = strongly agree to 5 = do not agree at all) questions (Appendix A). An independent expert on scientific survey development reviewed the validity and reliability (S.A.). We performed a pilot test to measure the feasibility of the survey by inviting five independent potential referring ROs. Semi-structured interview questions were asked to guide them in critically appraising the questionnaire (Appendix B), using the think-aloud method.

An in-depth interview topic list was developed based on the outcomes of the survey, and iteratively adjusted by multiple stakeholders until considered satisfactory (Appendix C). We planned interviews with ten ROs to obtain in-depth clues on the survey (n=6) (Appendix C) and behavioural psychology aspects (n=4) (Appendix D). Our previous research showed that psychological aspects have a great influence in radical innovation adoptions such as PT (10). For the latter, several theoretical constructs from behavioural change theory were used (14,15). In addition, we conducted seven interviews with patients to obtain information on the patient journey, and patient information (Appendix E). The results of the interviews were used to guide and set up the workshops.

Two workshops were scheduled with ROs for each of two specific cancer care pathways: lung cancer (n=7) and oesophageal cancer (n=10). Our interview respondents had defined these as being the most complex.

The workshops were designed according to the design thinking method, which consists of the steps empathise, define, ideate, design/prototype, test and implement (16). Participants in the workshops included two ROs and a manager from the PTC, and one or two ROs from each referring institute. The workshops were guided by two independent consultants with expertise in design thinking methodology. The first workshops were built around empathising, defining and ideating; we empathised by understanding the different perspectives and to identify pains and gains (barriers and facilitators) from all the participants. There was a major focus on empathising, based on the previous research stating the influence of the psychological aspect in PT adoption, and the importance of good communication and collaboration (10). This methodology allowed us to co-creatively identify new problem statements in a multidisciplinary way. The barriers were placed into the care pathway of the patient, and based on this, solutions were suggested and prioritised according to their originality and feasibility. The second workshops were planned to ensure collective action and ownership of the design, and practical application of interventions. Here, the participants collectively selected the solutions with the highest priority and designed for each intervention the SMART goal, concrete steps, necessary stakeholders, resources, expected barriers, investments and deadlines.

The study population for the survey consisted of all 330 referring NVRO members in the Netherlands (ROs, ROs in training and Physician Assistants (Pas)). They were approached in August 2020 via a weekly newsletter, and invited to participate. Referring members who confirmed participation, received
the survey with a unique code, to ensure anonymity and the possibility of repetition of the survey in the future. 
For the 17 interviews and the workshops, participants were selected using purposive sampling. ROs were approached via personal contacts; patients were selected who had recently been referred. Interviews were performed in 2021 and workshops were carried out in autumn 2021.

To analyse the data from the survey, descriptive statistics were performed in SPSS; the data were not normally distributed after removing unrealistic outliers. To compare means of academic RTCs, non-academic RTCs and RTCs connected to a PTC, a Kruskal–Wallis test was performed. To test the relation between the number of referrals and attitude (defined as the perceived relative advantages of PT by the referrers and their belief on the quality of scientific evidence on which the model-based approach is based on; questions 15, 17, 19 and 22, Appendix A) an X² test was performed. The interviews were transcribed verbatim using MS Word’s Dictate function and coded with NVivo, following the steps of open, axial and selective coding. The workshops were summarised by manual coding, following the same coding steps as in the interviews.

The study was approved by the Institutional Review Board (IRB) of Maastro, to ensure that the study was carried out according to the GDPR guidelines.

Results
Four of the five independent referring radiation oncologists invited participated in the pilot test to assess the quality of the survey questions. The suggested changes were adopted, which were mainly in connection with medical jargon and the structure of questions. Forty-two percent (138/330) of the respondents completed the survey; the majority were ROs (89%).

The main barriers identified through the survey were patients’ choice (n=47; 34%), followed by logistical reasons such as a too-long lead time for a plan comparison (n=37; 27%) and too limited added value (n=32; 23%). In a further analysis, three factors appeared to be related to the number of patients the respondents reported to have referred for PT: 1) The number of patients they mentioned to have referred was significantly higher amongst ROs who had a positive attitude than amongst ROs without a positive attitude (p=0.002); 2) Similarly, the number of patients they mentioned to have referred was significantly higher amongst ROs reported to have good knowledge of NIPPs than ROs that responded to have insufficient knowledge (p=0.042); 3) PTC-connected respondents said to have referred, on average, more patients than non-PTC-connected ROs responded to have referred (p=0.002).

From the interviews with ROs on the survey results (n=6), the barrier of logistics was accentuated (6/6), due to increased workload (transferring data to the PTC for plan comparison) resulting in longer lead time. Although the model-based approach was generally accepted (6/6), a major barrier mentioned by five respondents (5/6) was that some of the models did not select those patients they intuitively expected to benefit from PT and vice versa. This was especially the case for new indications such as oesophageal cancer. The perception of the current scientific evidence of PT and the need for an RCT was divided. Four participants (4/6) mentioned that more patients need to be treated with PT to obtain more evidence, whereas two others (2/6) suggested performing an RCT for patients selected based upon models of the NIPPs. The ROs expected that the most important barriers to patients were travel time (6/6) and the lack of information (3/6). However, four respondents (4/6) also believed that travel services would not entirely solve this problem for patients. Four respondents (4/6) mentioned that these barriers occur the least in the breast cancer care pathway, and the most in lung cancer (3/6) and oesophageal cancer (2/6). This is due to the complex logistics of concurrent chemo-radiotherapy and the impact of the physical condition. The interviews with ROs from a behavioural psychology perspective (n=4) showed that most concerns were raised on reactance and the threat of autonomy, which was mainly based around the pressure experienced by the PTCs to refer patients. In addition, the scepticism about clinical advantages was mentioned, and the lack of self-efficacy (someone being confident in their own abilities around PT). Furthermore, the lack of organisational readiness, feeling involved in the introduction of PT and the lack of knowledge to estimate the eligibility of the patient were mentioned. Scepticism about the new scientific method was mentioned least.
The patients \(n=7\) mentioned in the interviews that the main barriers were the inefficient coordination between the referring centre and the PTC \(7/7\), especially when the patient receives another treatment parallel to RT. In addition, patients \(7/7\) indicated that the communication on the care pathway and information provision could be improved by tailoring information to the specific patient. For example, this could happen through better visibility online through patient portals, improved shared decision-making with the doctors and the involvement of patient organisations. Furthermore, the long travel time was highlighted by the patients \(3/7\), especially having to arrange it themselves, as well as the discomfort during treatment due to travelling \(3/7\).

During the first workshop sessions, the main gains of PT mentioned were a lower risk of complications, better survival and the positive experience of being treated with the best and latest available treatment. Some of the barriers mentioned were the difficulties of travelling (including costs) that patients are faced with, patients being deprived from social networks, and complex planning and logistics. Other barriers were the uncertainty regarding the outcome of the plan comparison and the start of treatment, and the complexity of the care pathway. Also mentioned were changes in the treatment team and contact person, and delay. For the referring ROs, an important barrier was the workload related to referral for plan comparison and the uncertainty of the exact added value of proton therapy for an individual patient or for a specific patient group, for example patients with a poor tumour-related prognosis. In the second workshop sessions, the participants collectively decided on the interventions they wanted to implement to deal practically with the barriers.

A summary of the proposed interventions for the top five barriers collected in the survey, interviews and workshops is given in Table 2.

**Discussion**

We found that the main barriers to PT adoption were patient eligibility, complex logistics – leading to, among others, increased lead time – the difficulties of travelling, patients’ choice and discussion on the perceived added value of PT. For oesophageal and lung cancer, these barriers were further discussed in depth and several promising solutions were created with PT referring radiation oncologists (ROs) and PT Ros.

**Barriers and interventions**

Lung and oesophageal cancer appeared to have the same barriers; the care path and patient populations show some similarity.

For patient eligibility, two aspects played a role. First of all, despite that the indications protocols were communicated via conferences, meetings, newsletters, and papers, lack of knowledge remained a barrier. This can be explained by the model-based approach requiring profound knowledge to estimate which patients are eligible for PT. For some indications such as breast cancer, only a very small number of patients qualify for PT (17). Second, the model-based approach also appeared to be an important barrier, partly because it is a new method for providing scientific proof. The reason to use such an approach instead of an RCT is has often been described in scientific literature (10). Our participants in the workshop suggested the further selection of patients with an intuitively perceived benefit of PT. This was achieved by adding soft selection criteria such as age, polypharmacy, physical fitness and a good prognosis. This should result in fewer patients being referred for a plan comparison, while enhancing the chance of being eligible, i.e. having a positive plan comparison, such that the increased workload of referring a patient feels more justified. In the future, also a website where one can submit a contoured CT to generate an automated plan comparison would be very helpful. This development will however take several years.

Logistical hurdles were important barriers as well. First, the application of concurrent chemoradiotherapy considers careful planning as RT is applied in the PTC, whereas chemotherapy is given in another hospital. These hospitals are not always familiar to the PTC (only to the referring radiation oncologist), and the combination of daily appointments, considering travel time between locations, requires careful planning. Therefore, other medical disciplines need to be involved in the PT care path as well. Barriers for referral to conventional RT have been found in several situations (18,19). These include patient anxiety about toxicity, mistaken belief of efficacy and side effects by physicians and patients, and insufficient knowledge of the referral process and treatment safety. Although for PT, the
referrals are not from one medical discipline to another, other medical specialists in the multidisciplinary team, are still important stakeholders in the treatment decision process. This is because they refer patients for radiotherapy and have certain expectations. In addition, we found that the increased lead time due to the plan comparison, was a barrier. Therefore, some respondents suggested organising a plan comparison in their own centre. Sometimes poor logistics in the exchange of health information has proved difficult between hospitals. This is also stated in literature (20). A portal to exchange health information has proved effective in quickly exchanging patient data with other centres (21).

This research showed that travelling for PT was still considered a significant issue for patients. Previous research shows that palliative cancer patients are willing to travel to distant RT facilities, if healthcare providers share full information with patients and reduce the burden (22). In our study, specifically the discomfort and the problem of travel arrangements was mentioned. The proposed solution was to hire a case manager whose main task is to inform the patient about all travel and accommodation implications. The case manager also makes the necessary arrangements for the patients, such as travel and accommodation. Overnight hotel stays are reimbursed in the Netherlands just like the costs of travelling. This solution is already described in previous literature to assist the patients and their family in navigating through a complicated set of services and supports (23,24). Introducing a case manager has shown to improve physical functioning and the feeling of having a choice as a patient (24).

Regarding patient choice, the provision of information to patients on the clinical advantages is needed, for patients to consider PT as an option. Previous research shows that increased awareness on a collective understanding of risks and benefits increases the patient knowledge by 88% and allows them to make an informed decision (25). The implementation of shared decision making strategies is very likely to help as well (26–28).

With respect to perceived added value, it has already been indicated that discussions about the scientific method are influencing the perceived added value (10,29). An adoption plan for the new method, including good communication and frequent reflection, is therefore recommended to foster acceptance (10).

With respect to the presence of bias (30), our survey was subject to non-response bias because not all of the sample members who were eligible to participate responded (response rate 42%). This was despite using techniques such as sending an information letter prior to the survey, using department leaders to motivate survey response and ensuring follow-up actions. Possibly, the survey was mainly filled out by ROs with some experience with proton therapy. A low response rate is seen in many studies requiring response by health care providers (31–33). However, our response rate may also suggest a problem with ownership within the Dutch RT community with respect to PT referrals lagging. Nevertheless, we extended our research with interviews and workshops. By combining these methods, we were able to include more respondents and obtain different and in-depth insights. Although we cannot exclude selection bias for the interviews with the ROs, mitigation strategies were applied by inviting two referring ROs from each referring hospital and from each discipline. Also, selection bias for the interviews with the patients was limited by applying no specific criteria for inclusion except for treatment. Given the fact that the treatment was new and the number of eligible patients low, we approached patients from referring hospitals who were treated for lung or oesophagus in the year before the interviews. By using different sources (survey, interviews with radiation oncologists, interviews with patients, workshops) we feel reasonably confident that we succeeded in identifying the most important barriers and facilitators. Nevertheless we applied the concepts of strength of conclusions used by Sun et al, in which cautionary words (such as may or appears) indicate not such a strong conclusion as without any bias could have been drawn (34).

The strength of this study is that it is the first one to find the barriers in the adoption of PT and possible clues to address these barriers. These clues were jointly conceived by ROs from PTCs and referring centres. This has been achieved through three different methods of data collection. Besides the above described limitation of bias, another limitation of our study is that we could not draw conclusions on the referrals based on the different tumour indications as we limited the workshops to oesophageal and lung cancer. Because physicians from other medical disciplines, such as surgeons, lung specialists or medical oncologists, were not involved in this study we suggest that further research with other multidisciplinary
stakeholders is needed to obtain their perspective on current practices. The effectiveness of the interventions should be studied to determine which interventions are successful in tackling the barriers. More cost-effectiveness studies are recommended to evaluate the model-based indications. We also will schedule a follow up survey within one and two years to study whether the current barriers are solved.

**Conclusion**

Based on three methods of data collection, we were able to find barriers for access to PT in the Netherlands and to design interventions to address these barriers. These interventions consists of 1) adding intuitive criteria to simplify patient selection for the referring RO; 2) optimising the transfer of the plan comparisons in the care-path; 3) better patient information, and travel support via the employment of a dedicated case manager; 4) more attention to involve all medical specialists in the multi-disciplinary treatment of the patient; 5) and a plan to address psychological barriers and concerns about the added value of PT. These insights can help PTCs to undertake appropriate actions to offer all eligible patients this innovative treatment.
References


Figure 1. Study design of the mixed methods study.

Abbreviations: RO= Radiation Oncologist. NVRO = Nederlandse Vereniging voor Radiotherapie en Oncologie, i.e. Dutch Society for Radiation and Oncology

Table 1. Distribution of Proton Therapy (PT) patients referred by the Proton Therapy Centres (PT centres) itself and by other radiotherapy centres (RT centres) of patients treated with proton therapy in the Netherlands January 2018 – June 2022.

<table>
<thead>
<tr>
<th>Referring centre for PT</th>
<th>Number (n)</th>
<th>Percentages (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTC itself (4 centres)</td>
<td>2201</td>
<td>76</td>
</tr>
<tr>
<td>Other RT-centres</td>
<td>696</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>2897</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 2. Summary of mentioned barriers deducted from all three methods (survey, interviews and workshops), including interventions proposed in the workshops.

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Subcategories</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient eligibility</td>
<td>Lack of knowledge</td>
<td>Educate and train ROs from referring RT centres; involve ROs from referring centres in developing NIPPs; make easily accessible information on eligibility</td>
</tr>
<tr>
<td></td>
<td>Model-based indications</td>
<td>Add intuitive eligibility criteria; educate and train ROs from referring centres.</td>
</tr>
<tr>
<td>Logistics</td>
<td>Careful planning of concurrent chemo-and radiotherapy</td>
<td>Involve the other medical disciplines, such as medical oncologists, surgeons, pulmonologists, gastro intestinal oncologists.</td>
</tr>
<tr>
<td></td>
<td>Increased lead time due to plan comparison</td>
<td>Submit the delineated planning CT immediately to the PTC, to enable simultaneous treatment planning of PT and photon plan; non-PTCs make a draft PT plan.</td>
</tr>
<tr>
<td></td>
<td>Information exchange</td>
<td>Improve data exchange, reduce administration.</td>
</tr>
<tr>
<td></td>
<td>Communication</td>
<td>Communication between non-PTC and PTC at several steps in the care-path: i.e. a priori eligibility, progress of plan</td>
</tr>
<tr>
<td>Travel</td>
<td>Information and burden</td>
<td>Assistance in travel and stay-arrangements, including a tool with overview of solutions.</td>
</tr>
<tr>
<td>----------------------------</td>
<td>------------------------</td>
<td>------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Patients choice</td>
<td>Information and support</td>
<td>Install a case manager in the PTC; develop a decision aid; appoint a coordinating RO in the PTC for the referring RO.</td>
</tr>
<tr>
<td>Shared Decision Making</td>
<td></td>
<td>Educate the referring RO, manage patient expectation by already mentioning PT early in the care-path, in the multidisciplinary team.</td>
</tr>
<tr>
<td>Perceived added value of PT</td>
<td>Scientific evidence</td>
<td>Collect more evidence by recording outcomes of treated patients, validation of the models; consider designing RCTs.</td>
</tr>
<tr>
<td></td>
<td>Awareness</td>
<td>Knowledge-sharing between PTC and non-PTC, and also involve other medical professionals, such as medical oncologists, surgeons, pulmonologists, gastro intestinal oncologists.</td>
</tr>
</tbody>
</table>

**CONFLICT OF INTEREST STATEMENT**

Manuscript title: Clues to address barriers for access to proton therapy in the Netherlands.

The authors whose names are listed on the title page of this manuscript declare that they have no conflict of interest.

They have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers’ bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.