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Minimum data elements for the Australian Particle Therapy Clinical Quality Registry

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Abstract

Introduction: Construction of the first Australian particle therapy (PT) centre is underway. Establishment of a national registry, to be known as the Australian Particle Therapy Clinical Quality Registry (ASPIRE), has been identified as a mandatory requirement for PT treatment to be reimbursed by the Australian Medicare Benefits Schedule. This study aimed to determine a consensus set of Minimum Data Elements (MDEs) for ASPIRE.
Methods: A modified Delphi and expert consensus process was completed. Stage 1 compiled currently operational English-language international PT registries. Stage 2 listed the MDEs included in each of these four registries. Those included in three or four registries were automatically included as a potential MDE for ASPIRE. Stage 3 interrogated the remaining data items, and involved three rounds – an online survey to a panel of experts, followed by a live poll session of PT-interested participants, and finally a virtual discussion forum of the original expert panel.
Results: One hundred and twenty-three different MDEs were identified across the four international registries. The multi-staged Delphi and expert consensus process resulted in a total of 27 essential MDEs for ASPIRE; 14 patient factors, four tumour factors and nine treatment factors.
Conclusions: The MDEs provide the core mandatory data items for the national PT registry. Registry data collection for PT is paramount in the ongoing global effort to accumulate more robust clinical evidence regarding PT patient and tumour outcomes, quantifying the magnitude of clinical benefit and justifying the relatively higher costs of PT investment.

Key words: Delphi method; heavy ion therapy; proton therapy; registries; routinely-collected data.

Introduction

Construction of the first Australian particle therapy (PT) centre is underway, with clinical operations at the Australian Bragg Centre for Proton Therapy and Research (ABCPTR) in Adelaide set to begin in 2025. Establishment of a national PT registry is essential to set a robust foundation for consistent, reliable and relevant data

collection even before the first patient is treated, and pre-determined mandatory minimum data elements (MDE) are essential. Moreover, establishment of a national registry has been identified as mandatory for treating patients with PT that are to be reimbursed by the Australian universal health care system's Medicare Benefits Schedule (MBS). This was mandated by the Australian Commonwealth Government Medical Services Advisory Committee as outlined in the 1638 public summary document,[1] to improve the robustness of the cost-utility modelling associated with PT compared with conventional photon radiation therapy (RT). Patients can be registered whether they are treated by conventional photon therapy or PT.

The evidence base for PT is accumulating,[2–4] but due to limitations and barriers unique to PT, and the tumours thought to most benefit from PT,[5–7] further data are required to understand its role and value in the treatment of cancer. As more and more level I evidence is awaited, the value of other forms of evidence such as registry-based and database-derived studies based on real-world data is increasingly recognised.[8–10] The proposed registry in Australia, The Australian Particle Therapy Clinical Quality Registry (ASPIRE) seeks to provide a uniform approach to data collection, recording patient, tumour and treatment outcomes. The objective is to validate the health economic modelling as outlined in the MBS application for PT, as well as provide a source of evidence for future MBS applications to expand the clinical indications for PT in Australia. The registry will be conducted in collaboration with the Trans-Tasman Radiation Oncology Group (TROG).

For a country like Australia where the patient population for PT is relatively modest and many tumours likely to benefit from PT are considered relatively rare, the ability to join and be aligned with international partners in consistent data collection approaches, data items and data analysis is paramount to contributing meaningful results in PT research. Furthermore, collaboration and coordination between the different states and territories in Australia are imperative for a registry to be nationally representative. This has been demonstrated in endeavours such as the Prostate Cancer Outcomes Registry-Australian and New Zealand (PCOR-ANZ), which was established in 2015 and involves seven Australian states and territories as well as New Zealand. It has been able to monitor and report on prostate cancer clinical practice and patient outcomes on this wide bi-national scale.[11–13] It is also crucial that any new national PT registry harmonises with existing relevant national registries to link data and allow automation of data linkages and analysis in the future.

The objective of this study was to determine a consensus set of mandatory MDE for ASPIRE.

Methods

A modified Delphi and expert consensus process was completed via a three-stage process.

Stage 1 involved the compilation of currently operational English-language PT registries from around the world, including the United States (US), Europe, Singapore, and the United Kingdom (UK). Jurisdictions were contacted by email correspondence. The US Paediatric Proton/Photon Consortium Registry (PPCR, version 2017), the European Particle Therapy Network (EPTN, version 2019), and the UK (version 2020) registry database forms were supplied to the authors with consent to utilise them for the purposes of this work. There was an opportunity to discuss in detail the items included in the various registries and the approaches taken. Data items were tabulated according to patient, tumour, or treatment categories. Registry database forms were interrogated, and mandatory data fields were identified.

Stage 2 involved listing the core data items included in each of the registries and comparing between registries, determining which items were included in all, three, two or only one of the registries, respectively. Those included in three or four of the registries were automatically included as a potential MDE for the Australian registry.

Stage 3 involved interrogation of the remaining data items found in either one or two of the international PT registries. These are the items that were included in the modified Delphi approach. There were two iterative rounds. The first was conducted via an online survey to a panel of experts (members of the Royal Australian and New Zealand College of Radiologists (RANZCR) Particle Therapy Working Group (PTWG) and two Australia-based medical physicists with interests in both PT and patient outcome data mining analysis). Through this, data items were categorised by a predefined Delphi consensus agreement of at least 60%. Scores equal to or above this value, for either inclusion or exclusion as a MDE, determined the inclusion or not of items. The items which did not reach consensus were then presented through a second round of consensus discussions. This took the form of a live poll session during the PT session of the RANZCR Annual Scientific Meeting (ASM) 2022 in Adelaide, South Australia. MDEs were included if at least 60% of the audience reached a consensus. Based on feedback from the ASM audience, two existing state-based registries with an RT minimum dataset were also reviewed. The final step of the process involved discussion in a virtual forum of the original panel of Australian experts to determine by consensus the final MDEs, with consideration of existing RT minimum datasets available in NSW and Victorian registries.

Results

Stage 1

Appendix I lists the data items in the four registries considered, with items scored as present (1) or absent (2) (Stage 1). The PPCR contains critical fields representing 31 mandatory assessment data items, and these were

taken to represent the MDEs. The mandatory fields are not derived from tumour-specific assessment forms. The EPTN registry uses both generic and tumour-specific assessment forms (available for 5 tumour sites—Head & Neck, Breast, Lung, Oesophagus and Prostate). The EPTN utilises a tiered data field system from levels 1–3, with level 1 representing mandatory data, level 2 representing more extensive data still considered standard of care and level 3 representing additional data not considered standard of care and requiring further medical ethics approval. The level 1 data fields were taken to represent the MDEs and totalled 61 in total from either the generic or tumour-specific forms. The Singapore dataset contained 55 MDEs, and the UK listed 74 MDEs.

There were 123 different MDEs identified across the four international registries. Sixty-two were patient-related items, 20 were tumour-related items and 41 were treatment-related items.

Stage 2

Of the 123 data items, 12 were included in all registries, 30 in three registries, 37 in two registries and 44 in one registry. For the EPTN registry, the data item was deemed included if it was a level 1 mandatory data item in either the generic or the tumour-specific forms and represented 'EPTN overall'. The MDEs included in all or three registries, in total 42, were included for consideration for the MDE for the National Australian Registry (Table 1). These are listed in detail in Appendix II.

Stage 3

Eighty-one remaining data items were identified for further interrogation to achieve consensus.

The online survey to the panel of Australian experts was circulated to 14 people, of whom 11 responded (79% response rate) within the allocated time. Twenty-two (of the 81) data items reached at least 60% consensus for inclusion as an MDE. Forty-eight data items reached at least 60% consensus for exclusion, and 11 data items did not reach 60% consensus for inclusion or exclusion and were unresolved. The list of MDEs at this stage is presented in Appendix III.

The 11 unresolved data items were then presented as a live poll to a wider group of about 40 participants at

Table 1. The number of minimum data elements included in one to four international registries

	All registries	3 registries	2 registries	1 registry	Total
Patient factor	3	17	22	20	62
Tumour factor	5	4	4	7	20
Treatment factor	4	9	11	17	41
Total	12	30	37	44	123

the PT session at the RANZCR ASM 2022. 86% of the respondents were radiation oncologists, and the average number of participants per poll was 20. Three additional data items reached >60% consensus for consideration of inclusion as an MDE, one data item was excluded via consensus and the remaining seven data items did not reach consensus (Appendix IV).

A virtual expert forum was conducted to determine the final agreed MDE list. Seven of the original 11 respondents in stage 3 of the expert panel survey participated. Prior to the live interactive forum, pre-reading was sent in the form of the MDE list as it currently stood, as well as a summarised compilation of both the New South Wales and Victorian Radiotherapy Minimum Data Sets (reference) and any key data items included in these that were not yet included in the MDE.

The final list of MDEs is provided in Table 2 with commentary on some items on specific data field options for that item. The final list was determined by the following series of guiding principles:

1. Removing obvious duplicate data items with significant overlap in data entry.
2. Combining multiple data items into one overarching data item.
3. Consideration of the MDEs as a representation of the *bare minimum* for mandatory data collection and reporting for PT.
4. Acknowledgement that if a data item is not deemed a mandatory MDE, it can and will likely be included in a more comprehensive and non-mandatory registry.

Discussion

Development of a national PT registry is foundational to responsible clinical operations at a PT facility, supporting safe and effective delivery of patient care while facilitating vital research development and expansion of PT evidence. Establishment of the MDEs is central to this, and a consensus-derived approach from across Australia encourages engagement and inclusiveness. The mandatory MDEs set the foundations through which a more extensive registry framework can be built over time and with additional funding.

The number of data elements deemed mandatory is debatable and varied, as shown by the difference in MDEs across the four international PT registries interrogated, as well as in national radiotherapy MDEs across Australia. The Cancer Institute of New South Wales (NSW) outpatient radiation oncology data set comprises 17 MDEs, while the Victorian radiotherapy minimum data set is made up of 41 items. From the perspective of data analysis and research projects, a more expansive MDE list is appealing, allowing greater breadth and depth of mandatory data to be collected. However, this needs to be balanced with the practicalities of data input and the time and effort required in clinical practice to satisfy mandatory MDE requirements for each patient over

Table 2. The consensus list of MDEs proposed for ASPIRE

	Comments
Patient factor	
1. Patient ID	Unique identifier
2. Aboriginal Torres Strait Islander status	Mandatory in the Australian context
3. Postcode	Allows for determination of socioeconomic factors
4. Treating institution	
5. Referring institution	
6. Sex	Distinct to gender
7. Gender	Distinct to sex
8. Date of birth	
9. Recurrence status	No recurrence
	Local recurrence
	Regional recurrence
	Distant recurrence
10. Date of recurrence	Date
	Not applicable
11. Date of last follow-up or death	
12. Survival status	Alive with no disease or controlled disease
	Alive with active disease
	Dead
13. Cause of death	Secondary to disease
	Treatment-related death
	Other cause
14. Clinician reported radiation therapy toxicity	Worst acute toxicity grade + first date of toxicity
	Worst late toxicity grade + first date of toxicity
Tumour factor	
15. ICD-code	Encompasses tumour site and whether primary/metastatic
16. Diagnosis date	
17. Histology	
18. Laterality/bilateral	
Treatment factor	
19. Retreatment with possible overlap/reirradiation	
20. Modality	Photons
	Protons
21. Number of fractions	
22. Start date of radiation therapy	
23. End date of radiation therapy	
24. Prescribed dose	
25. Delivered dose	
26. Treatment on trial protocol	
27. Hospitalisation during treatment (dates)	

many years. Thus, as noted above the rationale for this final minimum data elements list of 27 items is to provide the *bare minimum* for mandatory data collection and reporting for PT and as the baseline for a more comprehensive and non-mandatory registry.

The purpose of this study was not to define each of the selection options available for each data item, though commentary is provided for some MDEs. This will form the basis of future work in building the registry, developing a detailed data dictionary and assigning the necessary electronic drop-down options available for each data item. Work is already underway with the establishment of the wider registry which consults with established national metadata standards and MDEs as described in METEOR.[14]

Enormous effort will be required in the IT infrastructure that will underpin the collection, input, storing and analysis of registry and/or MDE data as well as data linkage. Such work should link and extract data from already established national registries such as Births, Deaths and Marriages and the MBS system, in addition to state cancer registries, for ease of auto-population and national cross-system communication. The Australian Computer Assisted Theragnostics (AusCAT) program and network can provide support to develop this work.[15,16] TROG aims to establish the infrastructure in conjunction with national PT groups, whose members have the experience and technical know-how to establish the extended national registry envisioned.

In countries like the UK, the critical importance of data collection for PT was recognised early, as evidenced by their dedication to embed data collection into the daily clinical practice of their proton beam therapy (PBT) centre. Their novel model and underlying infrastructure has been described,[10] utilising electronic forms and data tree approaches including conditional logic, to minimise the time needed for data entry and optimise a user-friendly experience through its integration into clinical workflows.

Drawing on the experience of international partners not only unifies and encourages collaboration, but also ensures a level of consistency and alignment with other PT registries and wider radiation oncology scientific communities, enabling pooling of participant numbers for clinical trials and studies both retrospective and prospective, to be conducted for less common tumours. Short of randomised controlled trials for every tumour type treated with PT, there is a recognised need for alternative evidence-based methodologies.[9] Prospective data registries are an essential component of the 'cohort multiple randomised controlled trials' approach whereby a large cohort of patients are monitored prospectively for various parameters.[17] Such approaches have been able to provide insight into outcomes of under-studied patient populations, such as neurocognitive outcomes in paediatric brain tumour survivors treated with PBT as described in a recent study using the PPCR by Lawell et al.[18] The use of the PPCR has allowed the analysis of treatment approaches and outcomes for very rare tumours such as pineoblastomas and other supratentorial embryonal tumours treated with PBT or photon therapy.[19] Patterns, variability, and evolution of radiation therapy practices have also been analysed with

large cohort numbers derived from registry data, providing insight into how best to move forward into the future.[20,21]

Furthermore, as more PT centres in Australia are built and become operational, a pre-defined set of MDEs will ensure data on every patient treated with PT in Australia will be harmonised for robust reporting. This will permit an audit of PT practice in Australia, validating or challenging practice and facilitating cost-utility assessments. Robust data collection will facilitate Australia's contribution to international efforts in the model-based selection of patients best served by PT.[22]

International collaboration is already underway. The EPTN is an example of establishment of consortia to pool and compare outcome data for patients for whom prospective studies are not feasible. It was formed in 2015 in response to the increase in the number of clinical PT centres in Europe,[9,23] and is an official task force of the European Society for Radiotherapy and Oncology (ESTRO). The EPTN is one of three active European networks working in complementary fields of PT, the other two being the European Network for Light Ion Hadron Therapy (ENLIGHT) and the Infrastructure in Proton International Research (INSPIRE). Developed in 2012 by Massachusetts General Hospital, the PPCR is a multi-institutional registry of paediatric patients treated with PBT and photon radiotherapy aimed to expedite research and optimally define the role of PBT in paediatric cancer care.[24] The Royal Adelaide Hospital is the first site involved outside of the US and joins a growing consortium of 23 paediatric radiation centres, with over 4,100 participants enrolled across the sites.

A possible limitation of this study was that the expert panel was derived from RANZCR PTWG members and selected Australia-based physicists with PT and data mining interests and research activity. Furthermore, although 14 experts were identified, only 11 responded to the first modified Delphi round and then seven were involved in the final process step. The lack of an operational PT facility in Australia and therefore limited direct clinical experience in PT within the expert group may be a disadvantage. However, the authors felt it important that those directly involved in the determination of national MDEs be based in Australia for accurate contextualisation and to foster engagement across the country. It may be noted again that the authors had the opportunity to discuss in detail the items in the international databases with their providers before the process and the rationale for the determined Australian national MDEs, compared to the other registries' approaches, with that same group after the process.

In conclusion, the minimum data elements for the ASPIRE were partly informed by early comparison and discussion of the international registries considered in this work. They have been validated here via a modified Delphi and expert consensus process, resulting in 14 patient factors, four tumour factors and nine treatment factors, that is, a total of 27 MDEs. The MDEs provide the core mandatory data items for the national PT registry known as ASPIRE, which can be developed over time with TROG to extend data collection and link data already recorded in local and other national registries. Registry data collection for PT is paramount in the ongoing global effort to accumulate more robust clinical evidence regarding PT patient and tumour outcomes, quantifying the magnitude of clinical benefit and justifying the relatively higher costs of PT investment.

Acknowledgement

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Committee MSA. Public Summary Document Application No. 1638 – Proton beam therapy for paediatric and rare cancers. 2020.
2. Hwang EJ, Gorayski P, Le H *et al*. Particle therapy toxicity outcomes: a systematic review. *J Med Imaging Radiat Oncol* 2020; **64**: 725–37.
3. Hwang EJ, Gorayski P, Le H *et al*. Particle therapy tumour outcomes: an updated systematic review. *J Med Imaging Radiat Oncol* 2020; **64**: 711–24.
4. Ofuya M, McParland L, Murray L, Brown S, Sebag-Montefiore D, Hall E. Systematic review of methodology used in clinical studies evaluating the benefits of proton beam therapy. *Clin Transl Radiat Oncol* 2019; **19**: 17–26.
5. Bekelman JE, Denicoff A, Buchsbaum J. Randomized trials of proton therapy: why they are at risk, proposed solutions, and implications for evaluating advanced technologies to diagnose and treat cancer. *J Clin Oncol* 2018; **36**: 2461–4.
6. Group CPBCTS. Proton beam therapy – the challenges of delivering high-quality evidence of clinical benefit. *Clin Oncol* 2018; **30**: 280–4.
7. Glatstein E, Glick J, Kaiser L, Hahn SM. Should randomized clinical trials be required for proton radiotherapy? An alternative view. *J Clin Oncol* 2008; **26**: 2438–9.
8. Kahalley LS, Peterson R, Ris MD *et al*. Superior intellectual outcomes after proton radiotherapy compared with photon radiotherapy for pediatric medulloblastoma. *J Clin Oncol* 2020; **38**: 454–61.
9. Grau C, Baumann M, Weber DC. Optimizing clinical research and generating prospective high-quality data in particle therapy in Europe: introducing the European Particle Therapy Network (EPTN). *Radiother Oncol* 2018; **128**: 1–3.

10. Hwang E, Burnet NG, Crellin AM *et al*. A novel model and infrastructure for clinical outcomes data collection and their systematic evaluation for UK patients receiving proton beam therapy. *Clin Oncol* 2022; **34**: 11–8.

11. Evans SM, Millar JL, Wood JM *et al*. The prostate cancer registry: monitoring patterns and quality of care for men diagnosed with prostate cancer. *BJU Int* 2013; **111** (4 Pt B): E158–66.

12. Evans SM, Nag N, Roder D *et al*. Development of an international prostate cancer outcomes registry. *BJU Int* 2016; **117** (S4): 60–7.

13. O'Callaghan M, Papa N, Pase M *et al*. Patterns of care for prostate cancer treatment and improving outcomes – are national registries the answer? *BJU Int* 2021; **128** (Suppl 1): 6–8.

14. (AIHW) AIoHaW. METEOR Metadata Online Registry. 2022. [Cited 6 July 2022.] Available from URL: https://meteor.aihw.gov.au/.

15. Field M, Thwaites DI, Carolan M *et al*. Infrastructure platform for privacy-preserving distributed machine learning development of computer-assisted theragnostics in cancer. *J Biomed Inform* 2022; **134**: 104181.

16. Field M, Vinod S, Aherne N *et al*. Implementation of the Australian Computer-Assisted Theragnostics (AusCAT) network for radiation oncology data extraction, reporting and distributed learning. *J Med Imaging Radiat Oncol* 2021; **65**: 627–36.

17. Langendijk JA, Boersma LJ, Rasch CRN *et al*. Clinical trial strategies to compare protons with photons. *Semin Radiat Oncol* 2018; **28**: 79–87.

18. Lawell MP, Paulino AC, Indelicato DJ *et al*. Neurocognitive outcomes in pediatric brain tumor survivors treated with proton radiotherapy: a study from the Pediatric Proton/Photon Consortium Registry (PPCR). *Int J Radiat Oncol Biol Phys* 2022; **114**: 1074.

19. Koenig JL, Indelicato DJ, Ermoian RP *et al*. Treatment approaches and outcomes for patients with pineoblastomas (PBs) and other supratentorial embryonal tumors (STETs) treated with radiation therapy (RT): a study from the Pediatric Proton/Photon Consortium Registry (PPCR). *Int J Radiat Oncol Biol Phys* 2022; **114**: e479–e80.

20. Correia D, Dave R, Indelicato DJ *et al*. The evolution of proton brainstem constraints: a multi-institutional study from the Pediatric Proton/Photon Consortium Registry (PPCR). *Int J Radiat Oncol Biol Phys* 2020; **108**: e233.

21. Connor M, Paulino AC, Ermoian RP *et al*. Variation in proton craniospinal irradiation practice patterns in the United States: a Pediatric Proton Consortium Registry (PPCR) study. *Int J Radiat Oncol Biol Phys* 2022; **112**: 901–12.

22. Ahern V. Selecting patients for proton beam therapy. *J Med Radiat Sci* 2021; **68**: 2–3.

23. Weber DC, Grau C, Lim PS, Georg D, Lievens Y. Bringing Europe together in building clinical evidence for proton therapy – the EPTN-ESTRO-EORTC endeavor. *Acta Oncol* 2019; **58**: 1340–2.

24. Hess CB, Indelicato DJ, Paulino AC *et al*. An update from the Pediatric Proton Consortium Registry. *Front Oncol* 2018; **8**: 165.

Appendix I

Patient/tumour/treatment factors included ('1') or not included ('2') according to each international PT MDE list

Patient factors	PPCR	EPTN overall	Singapore	UK
Diagnosis	1	1	1	1
Treating institution	1	1	2	2
Referring institution	2	1	2	2
RO in charge	2	2	1	2
Gender	1	1	1	1
DOB	1	1	1	1
Age at diagnosis	2	2	1	2
Age at assessment	2	2	1	1
Age at first date of radiotherapy	2	1	2	1
Race	1	2	1	1
Ethnicity	1	2	2	1
Baseline health issues	1	2	2	1
Occupation	2	2	1	1
Patient ID	2	1	1	1
Contact person at PT centre	2	1	2	2
Date of registration	2	1	2	2
Date of consent	1	2	1	2
Family history of cancer	2	2	1	1
Smoking status	2	1	1	1
Smoking history (past, current, PYH)	2	1	1	1
Alcohol use	2	1	1	1
Baseline weight	2	1	1	1
Baseline height	2	1	1	1
Previous cancer	2	1	1	1
Previous cancer treatment	2	2	2	1
Most recent cancer treatment	2	2	2	1
Performance status	2	1	1	1
Menopause	2	1	2	1
Steroids	2	1	2	1
Anti-epileptics	2	1	2	1
Loss of weight	2	1	2	1
Cardiovascular co-morbidity	2	1	2	1
Abdominal surgery	2	1	2	1
TURP	2	1	2	1
IBD	2	1	2	1
Anti-coagulants	2	1	2	2
Bladder disease	2	1	2	1
Diabetes	2	1	2	1
Urogenital meds	2	1	2	2
Endocrinopathy	2	2	2	1
Hydrocephalus	2	2	2	1
Albumin	2	2	1	2
Hb	2	2	1	1
Neut	2	2	1	1
Lymphocytes	2	2	1	1
EBV DNA level at diagnosis	2	2	1	2
EBV DNA level at follow up	2	2	1	2
Follow-up—local recurrence	2	1	1	1
Follow-up—regional recurrence	2	1	1	1
Follow-up—distant recurrence	2	1	1	1
Date of last follow-up	2	1	1	1
Survival status	2	1	1	1

Appendix I. (continued)

Patient factors	PPCR	EPTN overall	Singapore	UK
Cause of death	2	2	1	2
Follow-up performance status	2	2	2	1
Metachronous primary disease	2	2	1	2
PROM toxicity	2	1	2	1
PROM QOL	2	1	1	1
Clinician reported RT toxicity	2	1	1	1
Clinician QOL	2	1	2	2
Chemo toxicity	2	1	1	1
Opioid use	2	2	1	2
Feeding tube	2	2	1	2

Tumour factors	PPCR	EPTN overall	Singapore	UK
Diagnosis	1	1	1	1
Diagnosis date	1	1	1	1
Date of first contact	2	2	1	2
Primary/metastatic	1	2	1	1
Tumour site	1	1	1	1
ICD code	2	1	2	2
Histology	1	1	1	1
Histological confirmation	2	1	1	1
Histological grade	2	1	1	1
Molecular typing	2	1	2	1
pStaging	1	1	1	1
cStaging	2	1	1	1
Paediatric tumour	2	1	2	1
Radiation related malignancy	2	2	2	1
Bilateral	2	1	2	1
Laterality	2	1	2	1
Diagnostic procedure	2	1	2	2
PET date at diagnosis	2	2	1	2
WBBS date at diagnosis	2	2	1	2
MRI date at diagnosis	2	2	1	2

Treatment factors	PPCR	EPTN overall	Singapore	UK
Proton technique (PS, IMPT, MFO, SFO)	1	1	1	1
Number of fractions	2	1	1	1
Start date of radiotherapy	1	1	1	1
End date of radiotherapy	1	1	1	1
Anatomic site/Radiation area treated	1	2	1	1
Total dose in cGy	2	2	1	2
Dose levels planned (number)	1	1	2	1
Total dose delivered for each dose level	1	1	2	1
Modality (protons)	1	2	2	1
Modality (photons)	1	2	2	1
Previous radiotherapy	1	1	2	1
Radiotherapy as adjuvant or neoadjuvant to surgery	2	2	1	2
Radiotherapy simulation date	1	2	2	2
Radiotherapy intent	1	1	1	1
Planning MRI	2	1	1	2
Planning PET or PET fusion	2	1	1	2
4DCT	2	1	2	2

Appendix I. (continued)

Patient factors	PPCR	EPTN overall	Singapore	UK
Target volume definition	2	1	2	1
Target volume cc	2	1	2	1
Total treatment days missed	1	2	2	1
Reason for treatment interruption	1	2	2	1
Anaesthesia/sedation	1	2	2	2
Motion management	2	1	2	2
Adaptive radiotherapy	2	1	2	2
Dosimetry	1	1	2	1
OAR dose	2	1	2	1
Treatment on clinical protocol	2	2	2	1
Treatment on trial protocol	1	2	1	1
Immobilisation	2	1	2	2
Fiducial type	2	1	1	2
Fiducial number	2	2	1	2
Spacer	2	1	2	2
Treatment sequencing (surgery, chemo, RT)	2	1	2	1
Systemic therapy	1	1	2	1
Systemic therapy details	2	1	2	1
Radio-isotope therapy	2	2	2	1
Stem cell transplant	2	2	2	1
Hospitalisation	2	2	1	2
Hospitalisation start date	2	2	1	2
Hospitalisation end date	2	2	1	2
Hospitalisation LOS	2	2	1	2

Appendix II

List of MDEs included in 3–4 international MDE lists

Patient factors
1. Diagnosis
2. Gender
3. DOB
4. Race
5. Patient ID
6. Smoking status
7. Smoking history (past, current, PYH)
8. Alcohol use
9. Baseline weight
10. Baseline height
11. Previous cancer
12. Performance status
13. Follow-up—local recurrence
14. Follow-up—regional recurrence
15. Follow-up—distant recurrence
16. Date of last follow up
17. Survival status
18. PROM QOL
19. Clinician reported RT toxicity
20. Chemo toxicity

Tumour factors
21. Diagnosis
22. Diagnosis date
23. Primary/metastatic

Appendix II. (continued)

25. Histology 26. Histological confirmation 27. Histological grade 28. pStaging 29. cStagingTreatment factors 30. Proton technique (PS, IMPT, MFO, SFO) 31. Number of fractions 32. Start date of radiotherapy 33. End date of radiotherapy 34. Anatomic site/Radiation area treated 35. Dose levels planned (number) 36. Total dose delivered for each dose level 37. Previous radiotherapy 38. Radiotherapy intent 39. Planning MRI 40. Dosimetry 41. Treatment on trial protocol 42. Systemic therapy

Appendix III

Included MDEs following online survey of expert panel

Patient factors

1. Diagnosis
2. Treating institution
3. Referring institution
4. Gender
5. DOB
6. Age at diagnosis
7. Race
8. Patient ID
9. Smoking status
10. Smoking history (past, current, PYH)
11. Alcohol use
12. Baseline weight
13. Baseline height
14. Previous cancer
15. Previous cancer treatment
16. Performance status
17. Follow-up—local recurrence
18. Follow-up—regional recurrence
19. Follow-up—distant recurrence
20. Date of last follow up
21. Survival status
22. Cause of death
23. Follow-up performance status
24. Metachronous primary disease
25. PROM QOL
26. Clinician reported RT toxicity
27. Chemo toxicity

Tumour factors

28. Diagnosis
29. Diagnosis date
30. Primary/metastatic
31. Tumour site
32. ICD code

Appendix III. (continued)

Tumour site

24.

33. Histology
34. Histological confirmation
35. Histological grade
36. pStaging
37. cStaging
38. Radiation related malignancy
39. Laterality/Bilateral

Treatment factors

40. Proton technique (PS, IMPT, MFO, SFO)
41. Number of fractions
42. Start date of radiation therapy
43. End date of radiation therapy
44. Anatomic site/Radiation area treated
45. Total dose in cGy
46. Dose levels planned (number)
47. Total dose delivered for each dose level
48. Modality (protons)
49. Modality (photons)
50. Previous radiation therapy
51. Radiation therapy as adjuvant or neoadjuvant to surgery
52. Radiation therapy intent
53. Planning MRI
54. Reason for treatment interruption
55. Anaesthesia/sedation
56. Motion management
57. Dosimetry
58. OAR dose
59. Treatment on clinical protocol
60. Treatment on trial protocol
61. Treatment sequencing (surgery. Chemo, RT)
62. Systemic therapy details
63. Radio-isotope therapy
64. Hospitalisation

Appendix IV

Results of the live poll session for 11 of the unresolved MDEs

Patient factors

- Ethnicity: No consensus
- Baseline health issues: 72% consensus for inclusion
- Date of registration: No consensus
- Family history of cancer: No consensus
- Loss of weight: No consensus
- PROM toxicity: 75% consensus for inclusion
- Clinician reported QoL: No consensus

Tumour factors

- Molecular typing: 83% consensus for inclusion
- Paediatric tumour: 75% consensus for exclusion

Treatment factors

- Target volume definition: No consensus
- Adaptive radiotherapy: No consensus