E-Survey: Current Status of Proton Beam Therapy in USA

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Abstract: The clinical use of Proton Beam Therapy (PBT) in the management of cancer is increasing worldwide. USA has high number of proton therapy centres and this number is growing with new proton therapy centres under development. This study expresses the views of Proton Therapy experts from 12 US cities based in 9 states with respect to the role of proton therapy in cancer treatment. An E-survey was conducted to assess clinical, technical, educational, and organizational resources and strategies in US -based Proton Beam Therapy facilities and to recognize patters of practice. The E-survey attempted to identify tumours which are more likely to benefit from Proton beam Therapy compared to Photon based Therapy. The role of Proton Beam Therapy in Breast, Brain and Lung cancers was also studied. The study also intended to find what improvements are needed to ensure efficient treatment planning, delivery and dosimetry. This is the first study of its kind in USA.

Keywords: Cancer, Proton Beam Therapy, Intensity modulated Proton Therapy, Single field uniform scanning, Quality Assurance, Synchrotron.

I. INTRODUCTION

The clinical use of PBT is increasing worldwide as it carries physical and dosimetric advantages over many photon based therapies. One of the most prominent advantages of PBT is non existence of exit dose. The benefits of PBT lie in its Bragg peak [1]. As protons travel through matter the energy deposition increases with depth giving rise to maximum energy deposition close to end of range of proton beam [1]. This maximum energy deposition is called Bragg peak and is followed by a region of sharp dose distal fall of. Readers are referred to articles on Proton physics for full description of Bragg Peak. Proton thus have a finite beam range. Photon beams on the contrary give rise to both entry dose and exponentially decreasing energy deposition with increasing depth resulting in exit dose beyond the target. Bragg peak can be placed inside the target thus sparing Organs at risk (OAR) beyond the target while providing maximum dose within the target. Other advantages of proton beam include low integral does, better sparing of organs at risk, potentially reduced risk of secondary cancer, Higher Linear Energy transfer (LET), Higher Relative Biological Effectiveness (RBE) and potential for dose escalation.

However PBT is not without its own challenges e.g. Proton beam range and dose calculations from CT Hounsfield units carry uncertainties [2]. Moreover Analytical algorithms are not very accurate for proton therapy due to steep dose fall offs. Proton therapy dose calculations are favoured by Monte Carlo algorithms. These uncertainties need to be accounted for in the Treating planning system (TPS). Proton beam therapy comes mainly in three forms i.e. i) Passive scattering (PS) including single and double scattering modes, ii) Uniform Scanning (US) and iii) Pencil Beam scanning (PBS). PBS results is reduced neutron production and scatter dose compared to Passive scattering techniques due to lack of scatterers and other beam modifying devices in the treatment head and nozzle. However PBS is more sensitive to tumour motion and thus require motion management techniques. There is considerable variations in use of Proton beam therapy in various cancers. More over there is lack of standardization of Proton beam quality assurance (QA) checks among proton beam therapy facilities. There is no survey conducted previously that compares and identifies technical, clinical, educational and organizational resources and strategies employed in PBT planning and delivery in multiple USA based PBT. No survey or study has previously identified improvements desirable in Proton Beam TPS, delivery and imaging system. Similarly no Study has previously attempted to find out views of PBT experts regarding how to improve education and knowledge of Staff in PBT facilities. In short, PBT is a complex and highly advanced treatment technique with many potential benefits and challenges. All of this warrants an E survey of various PBT facilities with respect to Treatment planning, types of tumours treated with PBT and types of tumours likely to benefit from PBT, image guidance and adaptive Proton therapy strategies employed in PBT facilities, Quality assurance and dosimetry, improvements required and education and training of staff. The E- survey was carried out in USA as USA has great number of Proton beam therapy

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facilities and thus PBT professionals have extensive Proton beam therapy experience. There is considerable variation in use of proton beam therapy among PBT facilities. This E-survey has attempted to understand the differences between various PBT centres regarding Proton beam therapy QA, Commissioning, planning, image guidance and delivery.

The objectives of this study are listed below:

1. Determine the current status of PBT in USA.
2. To evaluate clinical, technical, organizational resources and strategies that are employed in Proton beam therapy facilities in USA.
3. Find out which improvements in TPS and imaging system are desired as it is likely to improve patient treatment planning (TP) and delivery.
4. Identify how to improve staff education and training regarding PBT.
5. Ascertain what PBT skills are in demand now and in next 5 years.
6. Find out for which cancers PBT is suitable compared to Photon-based therapy.

The research paper is written for informed reader and prior knowledge of the medical terminology, proton beam therapy and Radiation physics is assumed. Definitions have been provided for more ambiguous terms in the glossary and in the text.

II. MATERIALS AND METHODS

Study Overview

This study captures the opinions of 15 Proton therapy experts working in 12 Proton Beam Therapy facilities based in 12 US cities. An E- questionnaire was designed to capture the opinions of Proton therapy experts regarding the role of proton therapy in treatment planning and delivery of various cancers. The E-survey was also intended to understand the education and training needs of the professionals in Proton therapy field as well as what improvements are desirable in the Proton therapy treatment. The study evaluated Proton therapy in twelve US Cities located in 9 US states.

The questionnaire was designed in MS word and consisted of 24 questions, most of which were close ended questions. Survey questions were structured in four sections namely i) Demographic Information, ii) Education and Training Information, iii) Quality Assurance and Dosimetry and iv) Proton Radiation safety. A sample questionnaire is shown in Appendix A under supplemental information. Social media Website platform (LinkedIn) was used to reach out the respondents and provide them with a Questionnaire and study participation invitation letter. The study was conducted in 2018-2020. The survey was conducted in two stages. The first survey was sent out in Jan 2018. In order to increase response rate, survey was again dispatched in Dec 2019. The last survey response was received in Jan 2020. A SWOT analysis was performed by analysing opinions of 15 Proton therapy experts about PBT. The designing of the survey, electronic distribution of the survey, collection of responses, and analysis of the data was managed by Principle Investigator (PI).

B. Ethical Consideration

This study was deemed IRB exempt as it was a quality enhancement and evaluation study. Responses were anonymous so no ethical approval was required. No patients were approached. No medical or personal data of participants collected. By answering the questionnaires, the professionals agreed to give their informed consent.

C. Target Population

This study is intended for those working in Proton therapy beam facilities (such as Radiation oncology and medical Physics experts working in PBT facilities) and those working in academia and industry dealing with proton therapy education and research.

D. Sampling

Non probability sampling is employed such as purposive sampling. This is because the target population (Proton therapy experts) are not easy to find and are rare as well as they are difficult to sample. The Principle Investigator has relied on its own judgement and knowledge when choosing target population e.g. PI knows proton therapy experts are likely to be found in PBT facilities, research centres and educational institutes. PI knows what expertise Proton therapy experts generally have and has used this knowledge to find participants for the survey. Purposive sampling allows the selection of sample of Proton therapy experts in PBT facilities and academic centres in USA.

PI considers Purposive (non-probability) sampling appropriate for this study as it allows selection of individuals that are particularly knowledgeable about proton therapy or have experience of proton beam therapy. Furthermore this technique allows selection of individuals who are willing to participate in the survey and are happy to share their opinions and experiences. Social media Platform Search tool was used to identify professionals with Proton therapy experience e.g. Search words such as proton therapy medical physicists were used to find Proton therapy experts in USA. Afterwards a connection request was sent along with a message to participate in the Survey. Most of these professionals became part of author's Network.

E. Statistical Analysis

Descriptive analysis was used to examine the results of the study.

F. Project Management

As it is a research project, project management and risk analysis aspects of this project are also discussed in Section VI and VII. Author of the present study has created a risk register that gives a good synopsis of the various risks anticipated in this project. A number of measures were taken to ensure good data quality.

G. Supplemental Data

Glossary and three Appendices are listed under supplemental data. Appendix A shows a sample E-questionnaire, Appendix B shows a list of PBT facilities and Appendix C provides abbreviations.

III. RESULTS

A. Response Rate

66 Proton therapy experts were contacted to participate in Proton therapy survey. A total of 15 proton therapy experts from 12 Proton Beam therapy facilities completed the E-Survey from 2019-2020. This gave rise to response rate of 22.7%. Four Radiation oncology experts had no proton therapy experience and declined to participate (6%) and 13 respondents (19.7%) agreed to participate in PT survey but did not return the filled PT survey. Thirty four (56.7%) professionals did not response to Proton Therapy survey invitation at all. Results are depicted in Figure **1**.

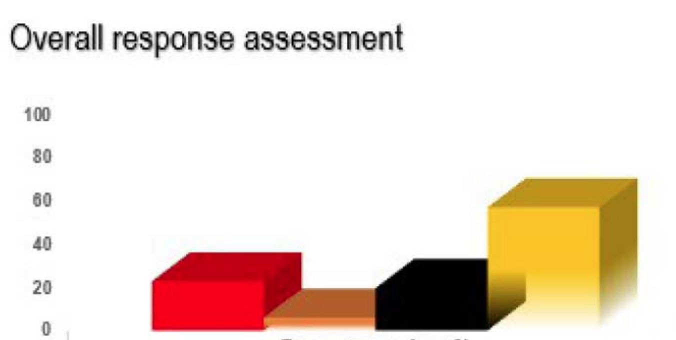
B. Respondent Characteristics

Results are shown in Figure **2**. Overall 40% of the respondents were females and 60% were males. As far as profession of the respondents is concerned 26.7% (4) were Proton Therapy Medical Physicists, 40% (6) were Medical Dosimetrist, 13.3% (2) were Proton Radiation Therapist, 6.7% (1) were Head of operations, another 6.7% (1) accounted for Radiation Oncology Clinical Supervisor and still another 6.7% (1) were Radiation therapist Intern. Each respondent is assigned a code as shown in Table **1**.

C. Proton Beam Therapy Facilities

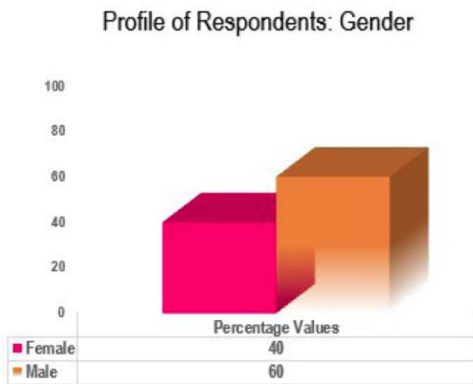
1. Work Experience

80% of the respondents had working knowledge of Proton Beam therapy whereas 20% of the respondents had both Theoretical and working knowledge. 26.7% of



	Percentage values %
PT survey filled & returned	22.7
Professionals with no PT Experience	6
Pofessionals who agreed to fill in PT survey but did not return the filled survey	19.7
Professionals who did not respond to PT survey participation request	56.7

Figure 1: Overall survey response rate.



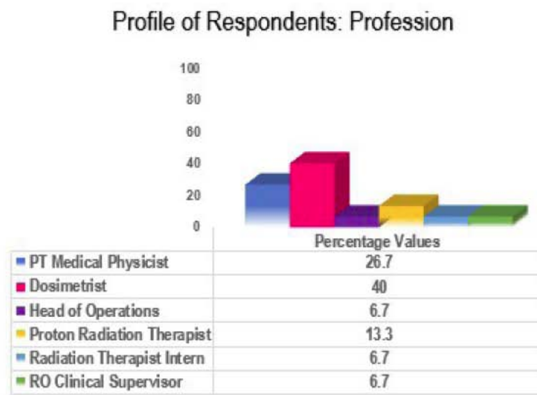


Figure 2: Socio-demographic profile of respondents.

Table 1: Respondent Codes

Respondent code	City/State (state code)	Profession
R1FL	Miami, Florida (FL)	PT Medical Physicist
R2MI	Royal Oak, Michigan (MI)	Medical Dosimetrist
R3TX	Houston, Texas (TX)	RO Clinical Supervisor
R4TX	Houston, Texas	Medical Dosimetrist
R5TX	Irving, Texas	Medical Dosimetrist
R6MA	Boston, Massachusetts (MA)	Radiation Therapy Intern
R7MA	Boston, Massachusetts	Medical Dosimetrist
R8OH	Cleveland, Ohio (OH)	Radiation Therapist
R9OH	Cincinnati, Ohio	Medical Dosimetrist
R10TN	Knoxville, Tennessee (TN)	Proton Therapy Medical Physicist
R11TN	Knoxville, Tennessee	Proton Therapy Medical Physicist
R12IL	Warrenville, Illinois (IL) & Somerset, New Jersey (NJ)	Medical Dosimetrist
R13IL	Warrenville, IL	Proton Therapy Medical Physicist
R14VA	Newport News, Virginia (VA)	Radiation Therapist cum dosimetrist
R15WA	Seattle, Washington (WA)	Head of operations

Note: RO = Radiation Oncology.

the respondents worked in a hospital, 20% in Proton Therapy centres (PTC) based inside a hospital and 53.3% in the Proton Centres. Results are shown in Figure **3**.

2. Location of the Institute and Type of Practice

Percentage of Responses received from professionals working in Proton Beam facilities based in 12 US Cities are shown in Figure **4**. Respondents who participated in the study worked in 12 different Proton therapy facilities. Appendix B shows the list of PBT facilities where survey participants worked. It was easy to derive the name of PBT facility from Geographical location of respondent work place as generally there is only one PBT facility in a particular region. Respondents did not show any interest in hiding their work location.

D. Type of Tumours Treated with PBT

All respondents said they treat Brain and prostate cancers in their Proton beam facilities. Overall 46.7% of respondents mentioned Other cancers. Other cancers included female breast, oesophageal, thymus, lung, chest wall, liver, chordoma (Brain), anal and mediastinum tumours. One respondent (R14VA) from Newport News, Virgina said in his centre no breast tumours are treated. 60% 0f respondents said they treat eye/ocular tumours, 86.7% said they treat

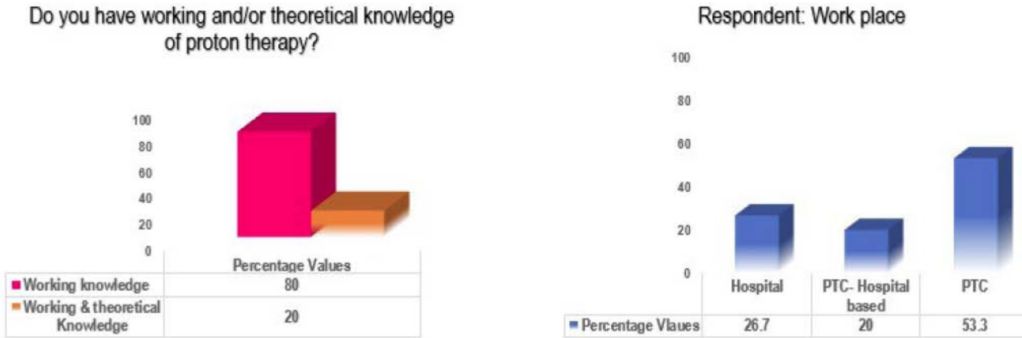


Figure 3: Clinical experience and type of work place.

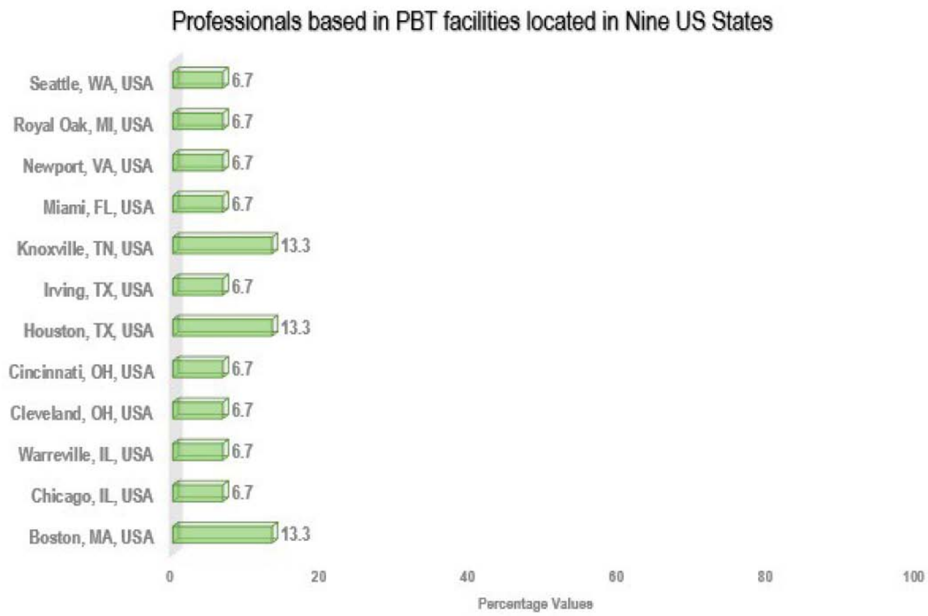


Figure 4: Area coverage of PBT facilities in USA.

sarcomas, 93.3% said they treat abdominal, HNC and CNS tumours. Results are shown in Figure **5**.

E. Proton Treatment Planning

1. Treatment Planning System (TPS)

Most of the respondents (53.3%) had RayStation® (RaySearch Laboratories) in their PBT facilities. 26.7 % respondents had Eclipse (Varian Medical Systems, Inc.). These respondents worked in Houston, TX, Cincinnati, OH and Newport News, VA (R3TX, R4TX, R9OH, R14VA). 20% had Elekta's XIO®. These respondents worked in Seattle, WA, Warrenville, Illinois, New Jersey and Boston, MA (R15WA, R12IL, R7MA). One respondent (6.7%) from Cleveland Ohio (R8OH) said they use Pinnacle (Philips) and one respondent (6.7%) from Boston, MA said Astroid Treatment Planning systems is used for treatment planning (R7MA). Two respondents were using two treatment Planning systems in their facilities i.e. R7MA from Boston, MA had both XIO and Astroid Treatment planning system in his facility. Similarly R13IL has two Treatment planning systems in their facility i.e. RayStation® for Pencil Beam and XIO for uniform scanning. Results are shown in Figure **6**.

2. Proton Treatment Planning Techniques

This question includes both methods of producing a clinical proton beam (e.g. PS, US and Active scanning) and methods of attaining adequate dose distribution (e.g. Single Field Uniform Dose -SFUD, Field patching, Intensity Modulated Proton Therapy-IMPT, Digital Edge Tracking-DET). Results are shown in Figure **7**.

One respondent (R80H) from Cleveland, OH said double scattering (DS) and DS with matching fields is used in her centre. Two (13.3%) respondents said they use Digital Edge tracking. Both these respondents worked in PBT facilities in Illinois (R12IL, R13IL).. One of the respondents R12IL also worked in New Jersey.

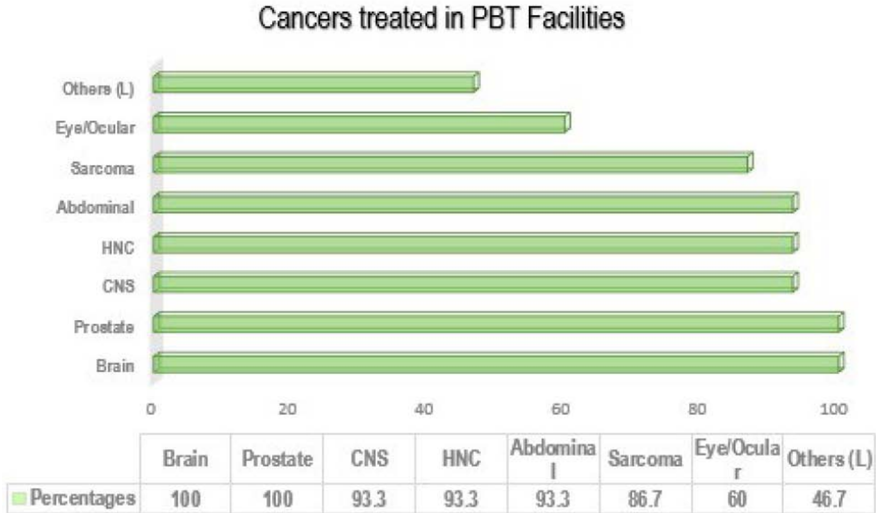


Figure 5: Types of Cancers treated with PBT in 12 facilities.

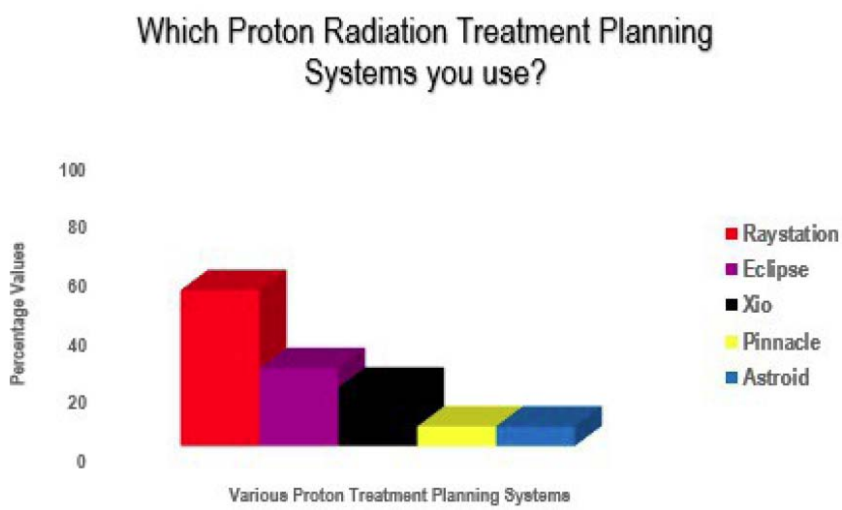


Figure 6: Different TPS in use.

Patch fields were used in four PBT facilities (26.7%) i.e. in 2 centres in IL, one centre in Boston MA and one in Newport News, Virginia. Four respondents (26.7%) said they use passive scattering in their PBT facilities. These respondents (R3TX, R5TX, R7MA, R14VA) work in PBT facilities in Houston, TX, Irving, TX, Boston, MA and Newport News, VA. All PBT facilities (93.3%) used SC except PBT facility in Cleveland, OH. Nine respondents (60%) said they use SFUD. These respondents worked in PBT facilities in Miami, Knoxville, Houston, Cincinnati, OH, Boston, royal oaks, and Warrenville. Ten respondents said they use SFUS (66.7%). These respondents work in Seattle, Knoxville, Houston, Cincinnati, Illinois, Boston, Newport News and Royal oak. Thirteen respondents (86.7%) said they use IMPT. These respondents work in PBT facilities in Seattle, Miami, Knoxville, Houston, Irving, Cincinnati, Illinois, Boston, Newport NEWS and Royal Oaks.

Sub-Group Analysis

Results for sub-group analysis are shown in Table **2**. The PBT facility in Cleveland, OH uses Image Guided Radiotherapy (IGRT), Adaptive Radiotherapy (ART), DS and DS with match fields. One Respondent (R9OH) working in PBT facility in Cincinnati, OH said IMPT, Single field Uniform Scanning (SFUS) , Single Field Uniform dose, IGRT, Spot scanning (SC) are used for Proton treatment planning. Two PBT facilities, one in Illinois and Somerset, NJ, use Digital Edge Tracking (DET). Besides DET, both PBT facilities also use IMPT, SFUS, Adaptive Radiotherapy (ART) , SC, patch and through (PTF) techniques. R13IL from Illinois also mentioned SFUD and IGRT. Both respondents from PBT facility in Houston TX said they use IMPT, SFUS, SFUD, SC and PS techniques. However R3TX also mentioned use of IGRT whereas R4TX also

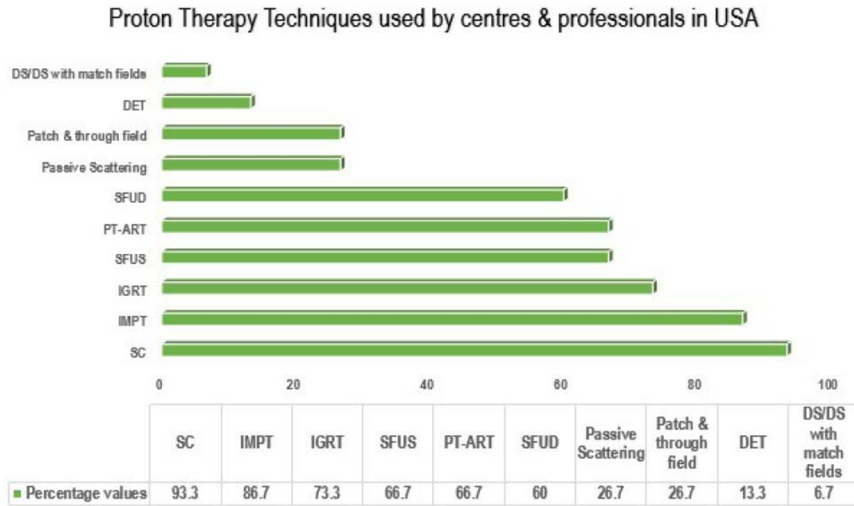


Figure 7: Treatment planning techniques in use by various PBT facilities.

Table 2: Treatment Planning Techniques in use by Region/Centre

Geo location of PBT facility	Proton Therapy Techniques used in the PBT facilities of Survey Participants
Miami, Florida (FL)	IMPT, SFUD, IGRT, ART, SC
Royal Oak, Michigan (MI)	IMPT, SFUS, SFUD, IGRT, SC
Houston, Texas (TX)	IMPT, SFU, SFUD, SC,PS, ART, IGRT
Irving, Texas	IMPT, IGRT, ART, SC
Boston, Massachusetts (MA)	IMPT, SFUS, SFUD, ART, SC, PS, PTF
Cleveland, Ohio (OH)	IGRT, ART, DS, DS with Match fields
Cincinnati, Ohio	IMPT, SFUS, SFUD, IGRT, SC
Knoxville, Tennessee (TN)	IMPT, SFUS, SFUD, IGRT, ART, SC
Warrenville, Illinois (IL) & NJ	IMPT, SFUS, ART, SC,PTF, DET
Warrenville, Illinois	IMPT, SFUS, SFUD,IGRT, ART, SC,PTF,DET
Newport News, Virginia (VA)	IMPT, SFUS, IGRT, SC, PS, PTF
Seattle, Washington (WA)	IMPT, SFUS, IGRT, ART, SC,

mentioned using ART. Respondent from Irving, TX said they use IMPT, IGRT, ART and SC techniques.

One Respondent ((R6MA) from Boston, MA said they use ART and SC whereas the other respondent (R7MA) also from the same PBT facility said they use IMPT, SFUS, SFUD, SC, PS and PTF. R6MA has limited experience with Proton beam therapy. She used PBT while working as a Radiation therapy Intern. Hence it seems PBT facility in Boston, MA use not only ART and SC but also IMPT, SFUS, SFUD, PS and DET. Both respondents from Knoxville, TN said they use IMPT, SFUD, IGRT, ART and SC. R11TN also mentioned SFUS use.

Respondent (R2MI) who have experience of working in PBT facility in Royal Oak, MI said they use IMPT, SFUS, SFUD, IGRT, and SC in their facility. Respondent from PBT facility in VA said they use IMPT, SFUS, IGRT, SC, PS and PTF. Respondent (R1FL) from PBT facility in Miami, FL said they use IMPT, SFUD, IGRT, ART and SC. Respondent (R15WA) from PBT facility in Seattle, WA said they use IMPT, SFUS, IGRT, ART and SC.

3. IGRT and Adaptive RT

Results are depicted in Figures **8-10**. Majority of the participants reported using Orthogonal KV/KV (66.6%) followed by Cone Beam CT (40%) to provide image guidance during Proton treatment planning and delivery. Use of Integrated MRI was reported by 20% (3) of the survey respondents.4D CT and Surface guidance use was reported by 6.7% (1) of the

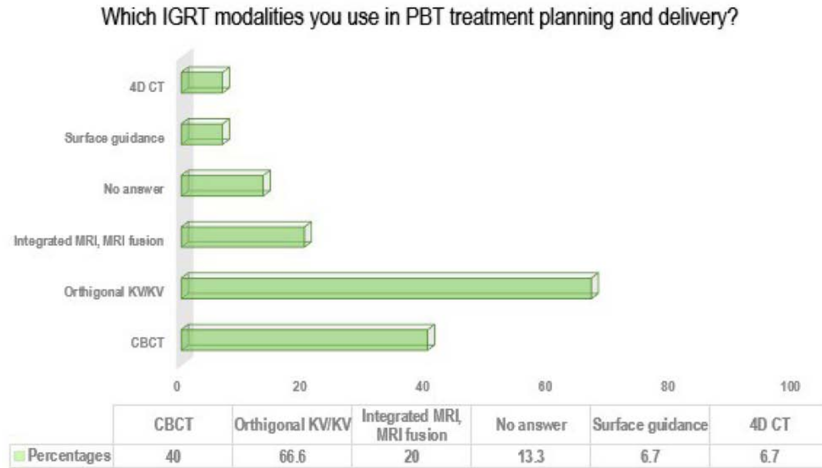


Figure 8: IGRT modalities in use.

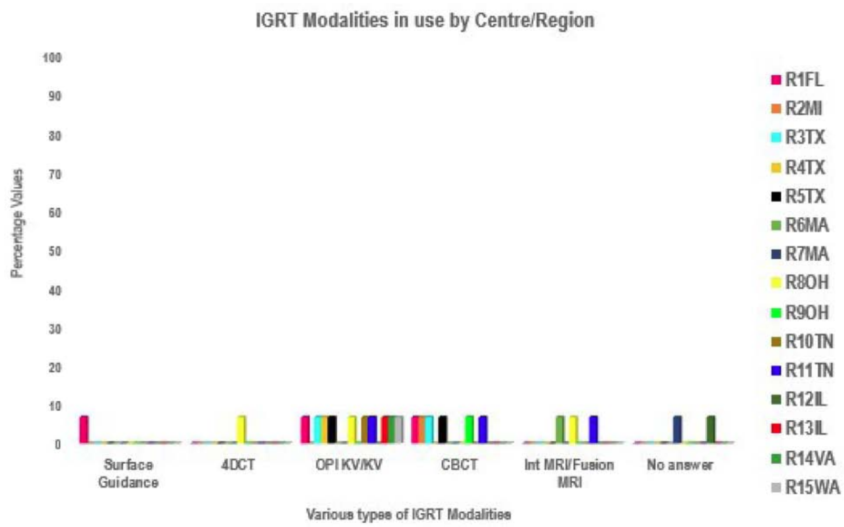


Figure 9: IGRT modalities: distribution of percentages by Region/centre.

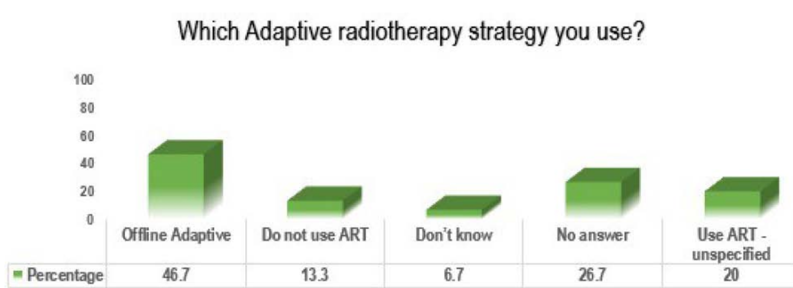


Figure 10: Adaptive RT strategies in use in PBT facilities.

respondents. As far as adaptive RT strategies are concerned majority of the respondents (46.7%) said they use offline Adaptive RT. 20% of the respondents said they use Adaptive RT but did not specify which Adaptive RT technique they use. 13.3% do not use Adaptive RT and 26.7% did not answer the question. One respondent (6.7%) said she does not know.

4. Skills and Expertise of Staff

4.1. Staff with Treatment Planning and Commissioning Skills

Results are depicted in Figures **11-13** and Table **3**. All survey participants (100%) said that they have staff with Proton treatment Planning, Commissioning and QA skills. 93.3% of the respondents said that

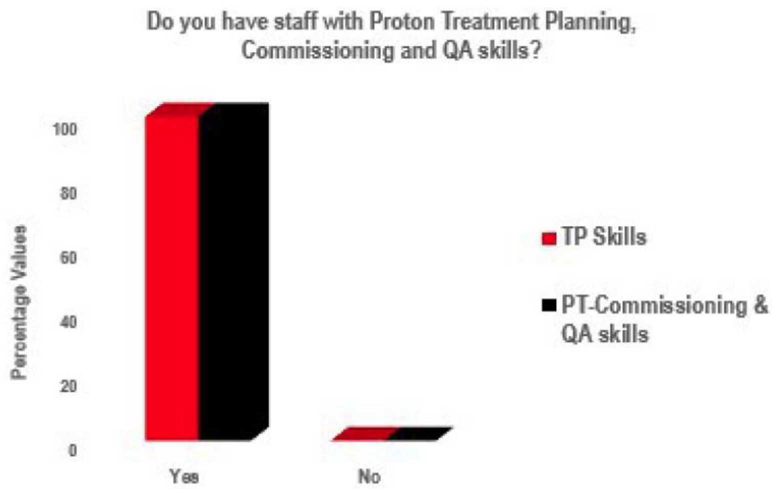


Figure 11: Staff with PBT skills.

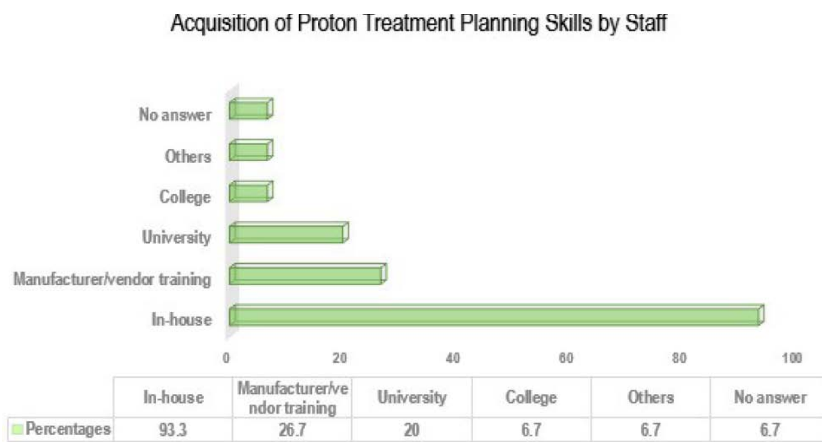


Figure 12: Different ways of acquiring of TP Skills.

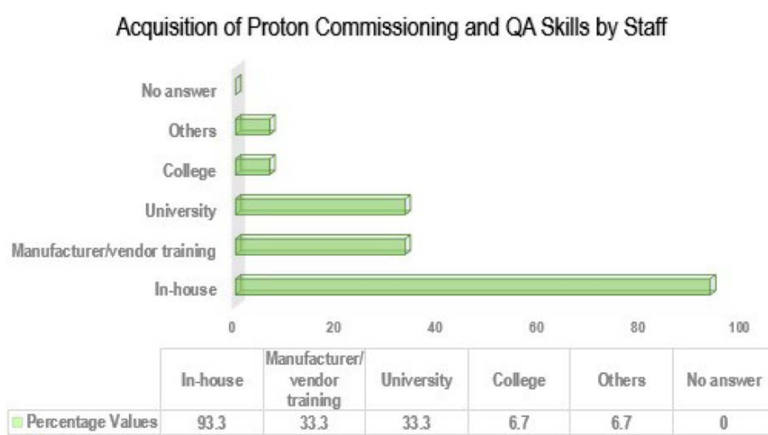


Figure 13: Different ways of acquiring QA and commissioning skills.

Treatment Planning, Commissioning and QA skills were acquired by in-house training. 26.7% and 33.3% of respondents Said Treatment Planning and commissioning skills/QA skills were acquired via vendor training respectively. 20% of the respondents said the staff acquired Treatment Planning skills from university whereas 33.3% of respondents said the staff acquired Commissioning and QA skills from University. 6.7% of the respondents said the staff acquired Treatment Planning skills, Commissioning and QA skills from college.

Table 3: Acquisition of PBT Skills by Region/Centre

Survey Participants	Acquisition of Proton Treatment Planning skills by staff	Acquisition of Proton Comm and QA skills by staff
R1FL	A	A, B,C
R2MI	A	A (Proton fellowship)
R3TX	A, C	A, B, C
R4TX	A	C
R5TX	A, B, C	A, B, C
R6MA	A	A
R7MA	A	A
R8OH	A	A
R9OH	A, B, C, D, E	A, B, C, D, E
R10TN	A	A
R11TN	A	A
R12IL	A, B	A, B
R13IL	A	A
R14VA	NO ANS	A
R15WA	A, B	A

Note: A = In-house training, B = Vendor/manufacturer training, C= University, D= College, E = Others.

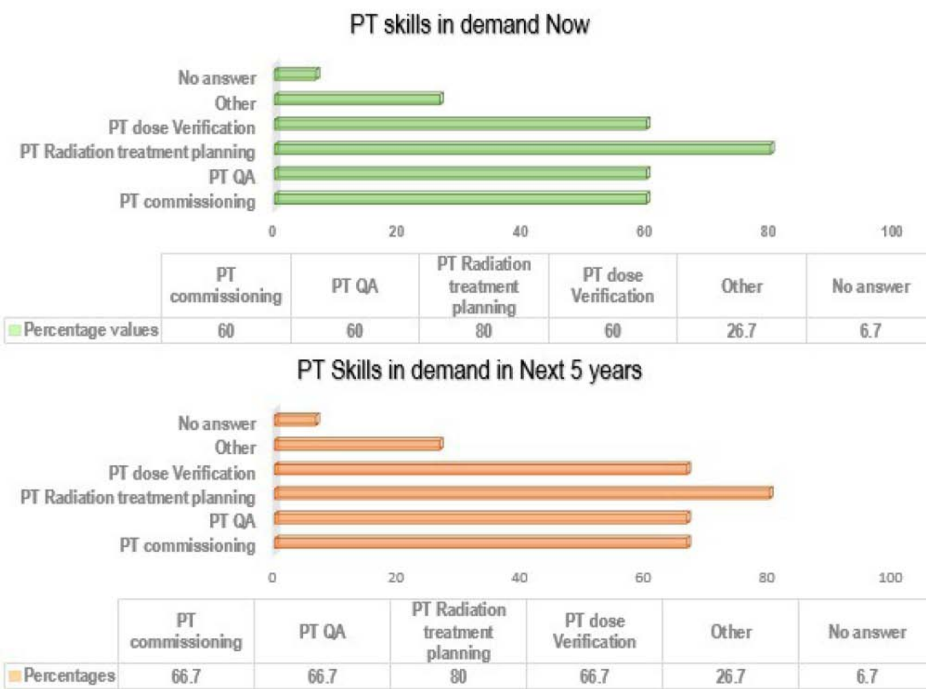


Figure 14: PBT skills in demand.

4.2. Skills in Demand Now and in Next 5 Years

Results are shown in Figure **14** and Table **4**. Majority of respondents (80%) said Proton Beam Therapy Treatment Planning skills are in demand now and in next 5 years. 60% of the respondents said Proton therapy dose verification, QA and commission skills are in demand now whereas 66.7% of the respondents said Proton therapy dose verification, QA and commission skills are in demand in next 5 years. 26.7% of respondents said other skills are in demand now and in next 5 years. Other skills included understanding of proton physics, ability to perform

Table 4: PBT Skills in Demand by Region/Centre

Survey Participants	PBT skills in Demand Now	PBT skills in Demand in next 5 years
R1FL	A,B,C,D,E (E=Proton Physics)	A,B,C,D,E (E=Proton Physics)
R2MI	A,B,C,D,E (E=Proton Arc Therapy)	A,B,C,D,E (E=Proton Arc Therapy)
R3TX	E (Continuous development of AI and Auto Planning in PBT	E (Continuous development of AI and Auto Planning in PBT
R4TX	C	E (Robust Optimization and LET optimization
R5TX	A,B,C,D	A,B,C,D
R6MA	A,B,C,D	A,B,C,D
R7MA	No answer	No answer
R8OH	C	A,B,C,D
R9OH	A,B,C,D	A,B,C,D
R10TN	C, E (Optimization knowledge, application specific to the TPS features scripting, Python UI scripting	C
R11TN	None at participant centre but all (A,B,C,D) skills in demand for new centres	None at participant centre but all (A,B,C,D) skills in demand for new centres
R12IL	A,B,C,D	A,B,C,D
R13IL	A,B,C,D	A,B,C,D
R14VA	A,B,C,D	A,B,C,D
R15WA	C,E(vendor specific training)	C

Note: A=Proton Therapy (PT) Commissioning, B= PT QA, C= PT Radiation treatment Planning, D=PT Dose Verification, E= other.

proton arc therapy, Optimization knowledge & Apps, UI scripting and Python programming skills. One respondent did not answer the question.

5. PBT vs. Photon Beam Radiation Therapy

In this section, Respondents were asked their opinion about which Proton therapy Planning techniques are better than Photon based 3D Conformal Radiotherapy (3DCRT), Photon-based VMAT and Photon based IMRT and for which body sites? Many respondents struggled in answering this question. 46.7% skipped this question whereas 53.3% answered the question. Results of their perspectives on comparison of PBT against photon Radiation therapy modalities are shown in Figure **15** and Table **5**.

F. Proton Beam Delivery System

Results are shown in Figure **16**. 66.7% (10) of the respondents said they use IBA Cyclotron, 6.7% (1) said they use Mevion S250, another 6.7% said they use Hitachi Synchrotron Probeat, still another 6.7% said they use Probeam. 13.3% (2) did not answer the question. IBA Cyclotron is used by professionals working in Proton Beam facilities in Seattle, WA, Miami, FL, Irving, TX, Boston, MA, Warrenville and DuPage, IL, Newport News, VA, Royal Oaks, MI, and Knoxville,

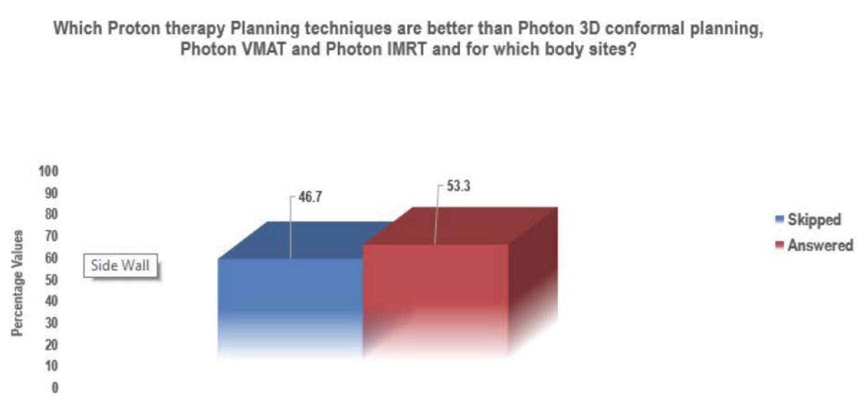


Figure 15: Distribution of percentages of respondents who answered Question on PBT vs. Photon RT.

Table 5: PBT vs. Photon RT

Cancers	Proton Therapy	VMAT-Photons	IMRT-Photons
All Cancers	IMPT is better in all aspects in terms of integral dose	VMAT & other IMRT techniques are better from a conformality perspective	IMRT should be used for boost dose
	IMPT is better in most cases except when metal or rapid density changes are present.	When pace makers are present near target, photons are opted for treatment.	
	Patient dependent, insurance approval		
	IMPT is better except for lung	VMAT is superior for Lung cancers	
	IMPT with blocks is better than photons		
CSI/ Paediatrics cancers	IMPT is good in SIB treatments.		
	IMPT better for some brain patients		
	IMPT better for brain patients to reduce dose to OAR.		
HNC	IMPT reduces use of Percutaneous endoscopic gastrostomy (PEG) tubes greatly.		
Female left breast cancers	IMPT results in better Heart sparing.		
	IMPT in certain situations: when heart is very anterior and within tangential fields even with DIBH		If minimal amount of lung and no heart in tangential fields.
	Better for internal mammary nodes		
Pelvic/Abdominal cancers	IMPT is better to reduce integral dose to protect normal tissues		

TN. Proton Beam Therapy facility in Cleveland Ohio uses Mevion S250 whereas PBT facility in Houston, TX uses Hitachi Synchrotron Probeat. Probeam is used by PBT facility in Cincinnati, OH.

G. Desirable Improvements

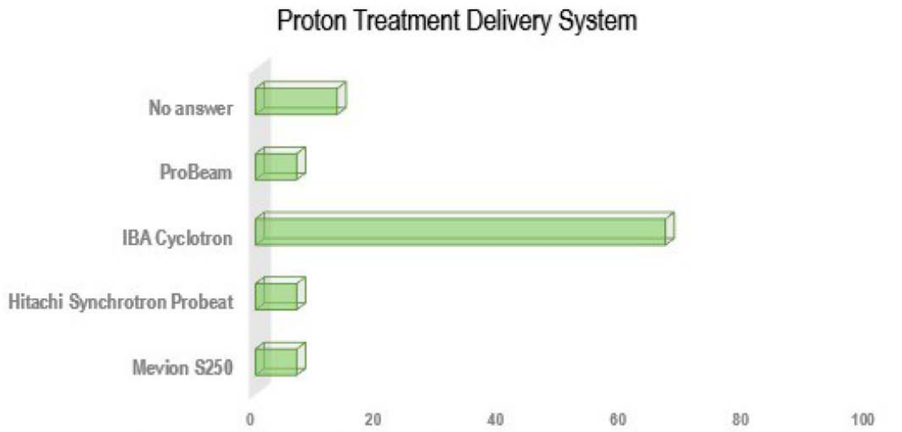
1. Improvements Desirable in Education and Training

In response to the Question how to improve Education and Training for Proton Beam Therapy, 12 respondents (80%) answered the question whereas 3 respondents (20%) skipped the question. Respondents provided lot of extremely good suggestions. These suggestions are depicted in the Figure **17** (The figure provides percentage distribution of the respondents who made a particular suggestion).

13.3% (2) respondents suggested vendor based training and more proton physics education are required. Other suggestions included Integration of AI and automation, train on similarities, PT education at university (Uni) level, more PT training for physicians, adding Proton therapy to curriculum, make licensure requirement, proton specific conferences and talks, quality process improvement projects, Live chat/talk sessions, standardized Proton certification courses, physics and engineering background and Self-directed learning.

2. Improvements Desirable in TPS

Results are shown in Figure **18**. Eleven (73.3%) respondents answered this question whereas four respondents (26.7%) did not. Respondents provided wide range of excellent suggestions to improve Proton beam therapy Treatment planning system and its capabilities. 13.3% of the respondents suggested faster Monte Carlo (MC) simulation, 6.7% of respondents suggested use of machine learning and another 6.7% suggested use of more automatic and less manual input options in TPS. Other suggestions included density correction tools, algorithm uniformity,



	Mevion S250	Hitachi Synchrotron Probeat	IBA Cyclotron	ProBeam	No answer
Percentages	6.7	6.7	66.7	6.7	13.3

Figure 16: Different types of proton beam delivery systems.

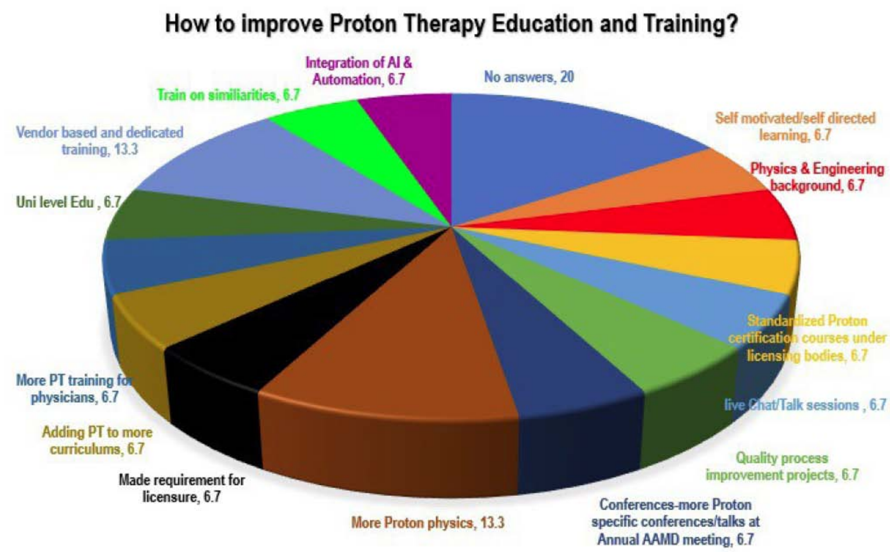


Figure 17: Suggestions for improving education and training of Staff.

improvement of contouring tools, Automation, auto segmentation, availability of more vendor related training, need for better workflow for replanning, better integration with treatment chair planning, availability of multicriteria optimization and need for user friendly adaptive planning modules, smaller spot spacing to achieve better optimization, Linear Energy Transfer (LET) dose modelling, faster GPU based calculations and faster spot scanning are required.

3. Improvements Desirable in Delivery and Imaging System

Results are shown in Figure **19**. Eleven (73.3%) respondents answered the question whereas 4 respondents (26.7%) did not answer. A number of good suggestions were made by Survey participants to improve Proton treatment delivery and imaging system. Majority of respondents (40%) suggested Implementation of in-room volumetric imaging/CBCT. 13.3% (2) of the respondents suggested use of faster layer switching times. 20% of the participants gave other suggestions. These suggestions included beam stability, motion management, 4D gating, better IGRT system, robotic couch adapted to posterior (POST) Oblique (OBL) fields, improved dose rate, higher reimbursement for proton therapy treatment and more insurance coverage for proton therapy patients.

H. Quality Assurance and Dosimetry

Results are shown in Figures **20-22**. 46.7 % respondents said they carry out QA checks whereas

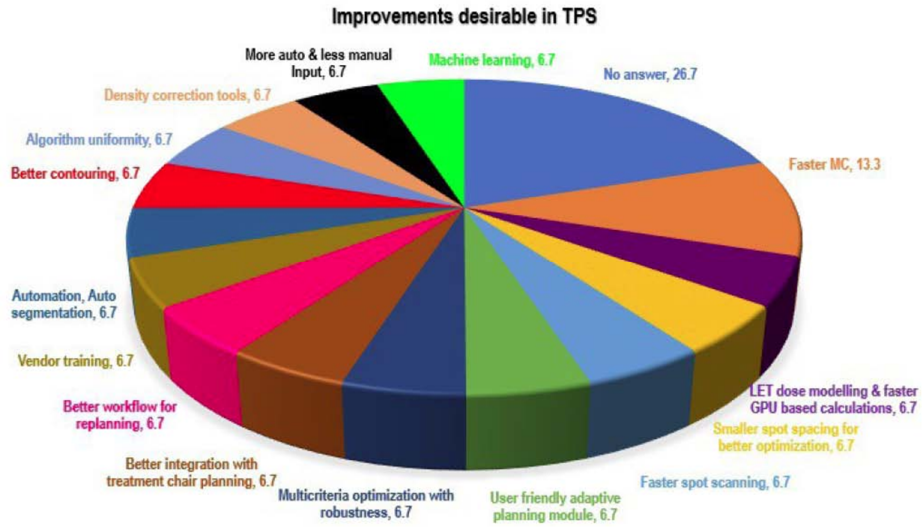


Figure 18: Suggestions for improving TPS features.

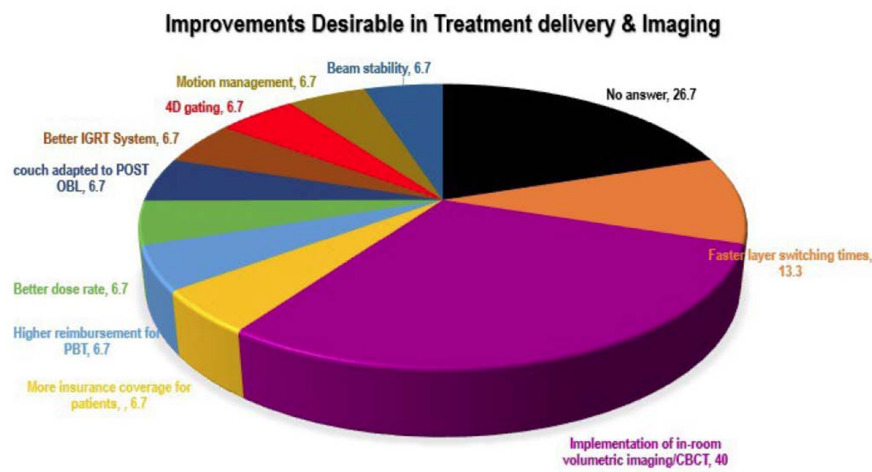


Figure 19: Suggestions for improving Beam delivery and imaging system.

53.3% did not answer the Question. No one said they do not carry out QA checks. Three respondents (3) said they do not carry out weekly QAs in their PBT facilities. They further added daily QAs are sufficient and are done on as needed basis. Three respondents (20%) said they carry out daily as well as weekly QAs in their PBT facilities. One respondent only mentioned daily QA and another respondent only said they do Daily and monthly QAs. With respect to dose verification devices majority of respondents said they use 2D dose verification. Daily QAs included laser alignment, table positioning accuracy, output, range/modulation accuracy, flatness/symmetry, energy check, spot position, imaging system (IS) consistency.

I. Radiation Safety

Results are depicted in Figure **23**. Majority of Respondents (33.3%) said no special qualifications required. A medical physicist can perform radiation safety tasks. Four respondents (26.7%) said dosimetrist or RTT can perform radiation safety duties. One respondent said basic radiation safety qualifications are required. One respondent (6.7%) said health physicist can do Radiation safety tasks and one respondent (6.7%) said same qualifications as Photon radiation required. Four respondents (26.7%) did not answer the question.

IV. DISCUSSION

This is first US based survey covering multiple Proton Beam Therapy facilities treating all cancers. 15 professionals from 12 different proton Beam Facilities participated in the survey. These centres are located in 12 US cities of 9 US states. The overall response rate was 22.7%. Studies comparing clinical, Technical, Educational and QA comparisons of Proton beam

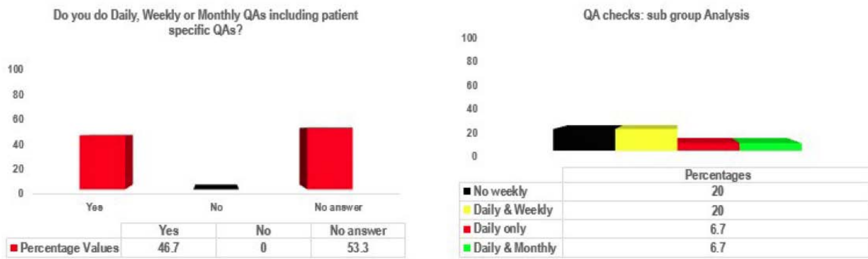


Fig. 20a

Fig. 20b

Type of QA done	Location of PBT facilities	n
No Weekly QAs done	Miami, FL, Knoxville, TN, *DuPage, Illinois*	3
Daily & Weekly QAs done	Cincinnati, OH, Boston, MA	3
Daily QA only done	Cleveland, OH	1
Daily & Monthly QAs done	Miami, FL	1

Fig. 20c

Figure 20: PBT QA.

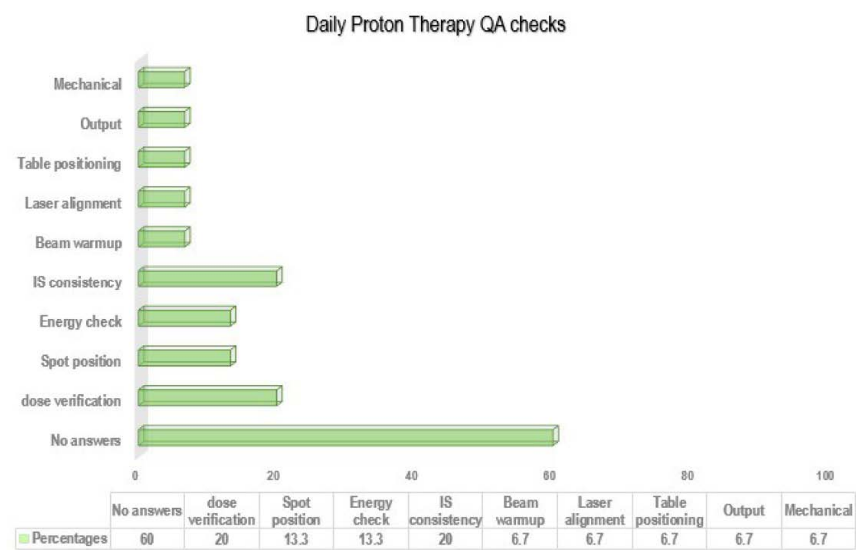


Figure 21: Daily QAs.

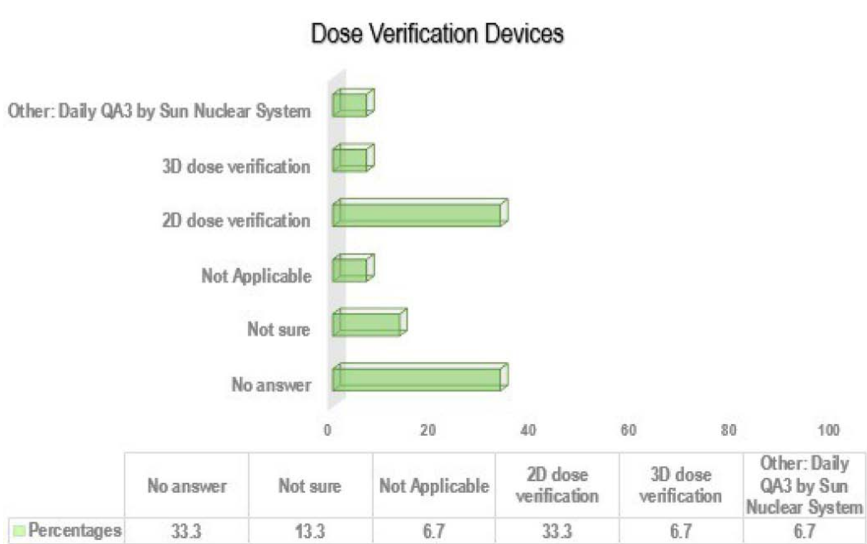


Figure 22: Types of dose verification devices in use.

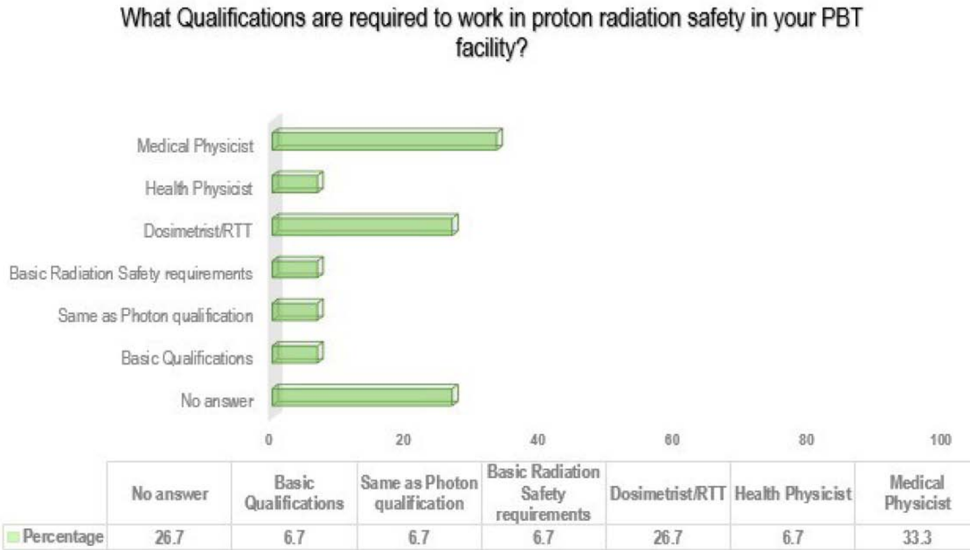


Figure 23: Qualifications required for radiation safety tasks.

Therapy among various US and non US based centres are missing. The current study has attempted to fill this gap in the literature.

A. Demographic Analysis

Majority of the respondents were male (60%). 40% of the respondents were Dosimetrist, 26.7% were Proton Therapy Medical Physicist, 13.3% were Radiation therapists, 6.7% were Head of operations, 6.7% were Radiation therapist Intern and 6.7% were Radiation Oncology Clinical Supervisor.

B. Clinical Aspects of PBT

All centres treated Brain and prostate cancers in their Proton beam facilities. Other cancers treated in the PBT facilities of participating professionals included Female breast, Oesophageal, Thymus, Lung, Chest wall, Liver, Chordoma (Brain), Anal and mediastinum tumours. This is the first study assessing use of proton therapy in all cancers not just one cancer type and for both adults and paediatrics tumours. According to a previous survey of paediatric tumour types in USA, most of the tumours treated were CNS tumours [3].

In terms of Proton beam treatment planning, Majority of professionals (53.3%) reported using RayStation TPS followed by Eclipse (26.7%), Xio (20%), Pinnacle (6.7%) and Astroid (6.7%) Treatment Planning systems in their PBT facilities.

Use of wide range of treatment planning techniques were reported by the professions in PBT centres. 93.3% of the respondents mentioned use of Spot (active) scanning to produce a clinical proton beam and 86.7% reported use of IMPT to achieve acceptable dose distribution. Successful use of Robust multi-field optimized IMPT with Dose escalated (66Gy RBE) SIB has been reported in treatment of locally advanced pancreatic cancer [4]. The three field arrangement (three non-coplanar beams from posterior and Right side or two oblique posterior beams plus a right sided non co planar beam) seems to decrease Normal Tissue complication probability of organs at risks in an intensified treatment giving rise to homogenous dose distribution in the target.

C. Other Clinical Aspects: Proton vs. Photon Treatment

In the present study Participants were asked to comment about which Proton treatment planning techniques are better than 3DCRT, VMAT and IMRT. Survey participants think PBT is better in all aspects in terms of integral dose for all cancers. Respondents also said that PBT is better for all tumours except lung. In view of the survey participants, for lung tumours VMAT is better than PBT. The present study also found that IMPT is better for brain patients to reduce dose to OAR and IMPT is better in SIB treatments. The present study also found that in views of survey respondents, PBT reduces the use of PEG tubes greatly.

Florin *et al*. [5] found that IMPT considerably improved dose conformity to Target volume compared to VMAT and IMRT leading to huge dose reductions in OAR (hippocampi, normal brain and volumes getting 20-30Gy in patients with skull based meningiomas. This may result in improvement of late neurocognitive side effects. The results of Florin *et al.* 2020 study are in line with our conclusion.

In a comparative study Adeberg *et al*. [6] found that PBT results in significant dose reductions in OAR (optical system, sub ventricular zone, Thalamus, hippocampus) in case of parietal tumours when compared to3DCRT and VMAT. In case of frontal lobe tumours, the highest dose reduction was observed in the mean dose to infratentorial normal brain, contralateral hippocampus, brain stem, pituitary gland, and contralateral optic nerve with PBT. In case of suprasellar tumours, PBT resulted in highest dose reductions in OAR such as Infratentorial brain, supratentorial brain and whole brain. This study concluded that sparing of OAR is dependent on intracranial tumour location.

A study by Dagan *et al*. [7] evaluated the mucosal toxicity in 23 Parotid cancer patients treated with median dose of 70Gy RBE. No grade 4 toxicity was observed and only one grade 3 dysphagia was reported. Grade 2 Xerostomia was observed in 14% of patients while 23% of patients experienced no xerostomia. No patient needed the feeding tube or intermittent intravenous hydration. These results are in line with the present PBT survey .

Holliday *et al*. [8] in a case matched control study of IMRT and IMPT in patients with Nasopharyngeal cancer found that patients treated with IMPT have reduced rates of Gastrostomy tube (GT)insertion due to better oral cavity sparing.

A review conducted by Musielak *et al*. [9] concluded that application of proton beam therapy in breast cancer treatment results in decreased cardiac risk events. A study conducted by Mast *et al*. [10] evaluated doses in OAR during IMPT irradiation with free breathing and IMPT with breath hold in 20 left sided breast cancer patients. The study compared results of IMPT with IMRT. The results showed IMPT resulted in nearly zero doses in OAR and thus in better cardiotoxicity. The breathing technique during irradiation did not result in reduced cardio-toxicity. A study conducted by Ares *et al*. [11] compared various 3D CRT, IMRT AND IMPT plans for 20 left sided breast cancer patients. The study concluded that considerable benefits were achieved with IMPT in terms of better PTV Conformality and decreased doses in OAR such as improved pulmonary and cardiac toxicity was observed in these patients.

According to a review article by Han [12] PBS is better than passive scattering in Lung cancer patients but there are a number of uncertainties associated with it such as uncertainties associated with beam range in lung heterogenous tissue. In addition to it intrafraction tumour motion also contributes to beam range uncertainties. PBS is much more sensitive to tumour motion that Passive scattering techniques. Therefore image guided motion management techniques are recommended such as 4DCT or gating.

D. Technical Aspects of PBT

Most of the professionals (66.7%) had IBA cyclotron in their PBT facilities. One (6.7%) respondent said they use Mevion S250 (synchrocyclotron), another respondent (6.7%) said they use Hitachi Synchrotron Probeat, and one respondent said (6.7%) said they use Probeam (Cyclotron). RayStation TPS supports various Proton beam systems such as Proteus from IBA, ProBeam from Varian, ProBeat from Hitachi, Hyperscan from Mevion, Sumitomo and ProNova [13]. This explains wide spread use of RayStation TPS in PBT facilities in USA. As far as Image guidance is concerned, most professionals mentioned use of Orthogonal KV/KV (40%) and CBCT (40%) in proton Beam treatment planning and delivery. Three respondents reported the use of MRI/Integrated MRI during treatment planning and delivery. One respondent mentioned use of surface guidance. Hrbacek *et al*. [14] also reported use of MRI for verification of geometric model during treatment planning of ocular disease in Proton Ocular centres. A report by Schulte [15] described the use of CT in Proton treatment planning due to its ability to provide electron density values needed to calculate range and dose. Electron density values are obtained by converting CT Hounsfield number. The report also mentions use of MRI in proton treatment planning as it provides better distinction between cancerous and normal soft tissue compared to CT. MRI is particularly used to define Planning Target volumes in High grade Gliomas as it permits distinction between GTV and oedema CTV, brain metastases and arteriovenous malformations. Schulte [15] also described use of PET in proton therapy planning for lung cancer as it allows distinction between tumour, scar tissue and positive mediastinal lymph nodes. With respect to image guidance in proton treatment delivery KV X-ray sources such as Onboard orthogonal imagers mounted on the gantry or nozzle along with imaging panel can be used to get diagnostic quality x-ray images matched to bony anatomy. Besides Orthogonal images, 3D volumetric

KV CBCT images can be acquired via gantry rotation. The gantry or nozzle mounted onboard imagers give rise to CBCT images [16]. Most of the respondents(46.7%) reported use of offline Adaptive Proton Therapy. 20% of the responded said they use Adaptive RT but did not specify further. With respect to image guidance in proton treatment delivery KV X-ray sources described the use of CBCT and Deformable Image registration for adaptive proton therapy. The Planning CT with better accuracy of Hounsfield Units was mapped onto CBCT that had less accurate Hounsfield units to create a virtual CT for proton dose calculations. Zhang *et al*. [17] has explained the use of 4DCT in adaptive Proton planning.

E. Organizational Aspects/Resources: QA and Dosimetry

PBT facilities have dedicated staff and time to carry out QA checks. The present study has found considerable variability in carrying out QA checks across the centres. Most professionals reported that they will perform QA checks daily (46.7%). Respondents from three centres (20%) said they do not perform weekly QAs as Daily QAs are considered sufficient. Three respondents (20%) said they carry out Weekly QAs in their PBT facilities. One centre (Miami, FL) carries out Daily and monthly QAs. Daily QAs included laser alignment, table positioning accuracy, output, dose, range/modulation accuracy, flatness/ symmetry, energy check, spot position, imaging system consistency. Patient specific QA or verification was not mentioned by any participant except one. Respondent from Miami, FL (R1FL) said that patient specific QAs are done on as needed basis. Considerable variability in QA process was also reported by Hrbacek *et al*. [14] where some centres carried out daily QAs, others weekly, some carried out monthly and some yearly QAs. Daily QAs carried out in Procure Proton Therapy centre, Oklahoma, USA Include Safety, mechanical, dosimetry and Imaging checks [18]. The dosimetry checks included Proton beam output, energy, and symmetry checks whereas imaging checks included image registration and PPS correction vector calculation. Other checks included couch movement, digital image panel position, Laser (Mechanical), door interlock, audio and video checks, Proton beam on light, Xray beam on light (Safety checks). rf-Daily QA3 device from Sun Nuclear Corporation, Melbourne, FL was used for daily QAs of Uniform scanning proton beam.

Actis *et al*. [19] describe a comprehensive daily QA check System called gantry 2 developed for Pencil Beam Scanning in Paul Scherrer Institute, Switzerland. The authors conclude that their daily QA takes 20 mins and eliminates the need for majority of the weekly and monthly QAs. This coincides with the results of the present study where weekly and monthly QAs are not as common as daily QA checks in many Proton Beam Therapy facilities.

AAPM Task Group 224 developed comprehensive QA guidelines for three proton therapy techniques namely, i) Scattering, ii) Uniform Scanning and iii) Pencil Beam Scanning which were published in Report No. 224 [20]. AAPM divides QA checks into 3 categories i.e. Equipment functionality/machine QA, Patient-specific QA and Treatment Planning System QA. AAPM further sub divides Machine QAs into 4 sub categories i.e. i) dosimetry parameter checks, ii) mechanical, iii) imaging system checks and safety checks. Daily QAs recommended by AAPM include output constancy, depth verification (distal and proximal), SOBP (spread out Bragg peak), width and spot position (dosimetry checks), couch translational motion, laser position accuracy, X-ray vs. laser isocentre, x-ray and proton beam isocentre coincidence, image acquisition, communication and CBCT. AAPM also recommend a number of safety QAs such as door interlock, audio and video monitor, beam and x-ray on indicator, monitor unit and collision interlocks, emergency motion stop, clear and pause buttons, optional tests include range modulation wheel timing, field light and width, dose rate, gantry angle read out accuracy, proximal depth verification, SBP width, field symmetry and flatness, interlock test therapy delivery and verification [20]. According to The National Association for proton therapy [21] there are 36 PBT facilities operational in USA. The current E-survey covers 33.3% of these centres. This is quite good coverage of PBT facilities in USA. The results of the present study show clinical, technical and educational patterns of PBT which are similar among 15 PBT facilities and areas where improvement is required.

F. Organizational Aspects/Resources: Staff Education and Training

All PBT facilities surveyed in this study have staff with proton treatment planning, commissioning and QA skills. Majority of the respondents (93.3%) said staff acquired these skills in-house. Staff of PBT facilities also used other modes to acquire proton skills such as vendor imparted training, via university and college courses. Besides treatment planning, dose verification, QA and commissioning a number of other important skills are also in demand. Other skills that are in demand include understanding of proton physics, ability to perform proton arc therapy, optimization knowledge and Apps, UI scripting and python programming. Thus, PBT facilities need to focus on providing training that includes these other important skills as well in order to ensure staff knowledge and experience is up to date and to ensure proton beam therapy can make most of the evolving and advanced technologies to improve patient treatment.

V. SWOT ANALYSIS OF PBT STATUS IN USA

Table **6** is a description of SWOT Analysis of PBT status in USA.

VI. LIMITATIONS OF THE STUDY AND FUTURE DIRECTIONS

The results of the present study are based on 15 survey responses received from Proton Beam therapy Experts working in major 12 Proton Beam Therapy facilities in USA. Rest of the PBT facilities in the US did not participate in the study. Although the findings are

Table 6: SWOT Analysis of PBT Status in USA Based on Opinions of Proton Therapy Experts

Strengths	Weaknesses	Opportunities	Threats
Majority of centres use spot scanning (93.3%) followed by IMPT. This is likely to result in reduced neutron production and low integral dose to patient	26.7% of the respondents said they use passive scattering technique. This technique is associated with increased integral dose to patient.	The survey participants made suggestions to improve education & training of staff. All these suggestions can be taken as opportunities e.g. vendor based training and more proton physics education needs to be provided. Integration of AI and automation, Adding PT to curriculum, more proton therapy conferences. standardized Proton certification courses	PBT Facilities are not well distributed. More centre are required in each state to improve patient access to this technology
The survey has shown that a great number of treatment planning techniques are used. This ensures better treatment planning for difficult tumours.	Variations in QA frequency and tests.	Suggestions were made to improve TPS. Again these suggestions can be taken as opportunities e.g. development of density correction tools, more automation, LET dose modelling abilities. Development of faster spot scanning abilities. Development of faster MC dose calculations	Lack of understanding of proton physics, ability to perform proton arc therapy, Optimization knowledge & Apps, UI scripting and Python programming skills. These skills are in demand.
40% of the respondents said they use KV/KV and CBCT for image guidance. This shows access to better soft tissue delineation and 3D volumetric imaging capabilities during Treatment delivery. This in turn ensures better patient and beam alignment reducing setup errors and errors due to tumour motion	Lack of in room 3D imaging.	Improvements desired in imaging and delivery system can act as opportunities e.g. faster layer switching times, development of 4D gating, development of robotic couch adapted to post oblique fields. Implementation of in room volumetric imaging	
46.7% of the respondents said that they use offline Adaptive RT planning with protons. This shows more centres are able to offer patient tailored treatment- again reducing errors in treatment delivery due to tumour shrinkage or patient weight loss. This also means better sparing of OAR.	13.3% of respondents said they do not use adaptive RT.	Development of systems that provide higher imbursement for patients. More insurance coverage for patients.	
PBT is used for a wide variety of cancer types.	Lack of insurance coverage for patients requiring PBT.		
Use of various commercially available TPS.	Complex treatment planning techniques		
Enough Staff with Proton treatment Planning, QA and commissioning skills.	Some cancer patients benefit better from photon based therapies e.g. VMAT is superior for Lung cancers		

correct but limited by small number of responses. However these responses came from major PBT facilities in US with extensive PBT experience. Studies involving more Proton therapy institutes and proton therapy experts are needed.

VII. CONCLUSION

The current E-survey covers 33.3% of PBT facilities in USA i.e. it covers 12 cities in 9 USA states. The study captured the opinions of 15 Proton Beam Therapy experts working in major 12 PBT facilities in U.S. Although results from this survey give a pretty good indication of the current status of the Proton beam Therapy in USA, results need to be generalized with care. Overall survey response rate was 22.7%. 60% of participants were male whereas 40% were female. Participants belonged to various professions with highest number of respondents were dosimetrists. Majority of centres in the survey used Spot scanning (93.3%) followed by IMPT planning technique (86.7%). Various IGRT techniques are used by these centres. Most common IGRT technique is- KV/KV and CBCT (40%). Most common form of Adaptive RT employed in these centres was offline adaptive RT (46.7%). IBA cyclotron was found to be the most common PT delivery system (66.7%) in use. A number of very useful suggestions to improve education and training of Proton therapy were made by the participants. Participants in the survey want to see improvements in RT treatment planning and delivery systems. 46.7% of the participants used daily patient specific QA. 2D dose verification systems were most commonly used (33.3%). PBT is used for almost all cancers including Brain/CSI, HNC, breast, prostate, abdominal cancers, sarcoma. As far as Radiation safety qualifications for proton centres are concerned, majority of respondents (33.3%) said physicist qualifications are required to carry out radiation safety duties. 26.7% said dosimetrist and RTTs. A number of measures were taken to ensure good data quality.

VIII. MANAGING INNOVATION

Project Delivery

Project was carried out and delivered in an innovative manner i.e. Online Social media website was used to reach out to the Proton therapy experts in USA and for data collection.

Project was delivered on time, with minimal budget and to the required standard.

IX. PROJECT RISK ANALYSIS AND DATA QUALITY

How Risks were Identified

Risks were identified using following techniques/tools

- WBS (work breakdown structure)
- Study similar E-Surveys to identify risks involved: Unfortunately no similar studies have been found.
- Study Clinical Trials and survey research to identify risks involved in surveys and Clinical research.
- Use of databases e.g. PERIL database
- Relevant experience
- Industry practice
- Published literature

Output

This identification process provided a list of identified risks. These risks are listed in Table **10**.

Risk Analysis Technique

Risk analysis was performed using qualitative risk analysis method.

Table 7: Probability of Occurrence

Score	Descriptor	Probability Rating
5	Almost certain	The event is very likely to take place
4	Likely	The event will possibly take place in majority of cases
3	Occasionally	The event could occur at some point in time
2	Improbable	The event has not happened but could happen at some point in time
1	Rare	The event may take place in some extraordinary circumstances

Source: Author.

Table 8: Impact Scale

Level	Descriptor	Detail Description
5	Extreme	Considerable loss of reputation, study terminated, considerable breach of ethics and good research practices
4	Major	Require retraction of published article, severe negative publicity. Study objectives could not be achieved. Results Invalid, results tempered with
3	Moderate	Study need to be repeated, irrecoverable loss of data. Reconstruction of database, loss of information/data due to loss of access to social media website
2	Minor	Little Financial loss, study could not be completed on time, Failure of word processing software or computer hardware.
1	Insignificant	No damage to reputation, Minor delay in completing the research project, No financial loss, Complaints that can be dealt in a routinely fashion.

Source: Author.

Table 9: Calculation of Risk Rating

Impact on project objective						
	Probability	**Insignificant**	**Minor**	**Moderate**	**Major**	**Severe**
		1	**2**	**3**	**4**	**5**
5	**Almost Certain**	L	M	H	E	E
4	**Likely**	L	M	H	E	E
3	**Occasionally**	L	M	H	E	E
2	**Improbable**	L	L	M	H	H
1	**Rare**	L	L	M	M	H
	Each risk is rated based on its probability and Impact.					

Source: modified [23].
Key: E: Extreme Risk, needs urgent action; H: High Risk, regular monitoring required; M: Moderate Risk: risk management process must be specified; L: Low risk, handle by routine procedures, No significant concern.

Table 10: Risk Register

Risk	What can go wrong If risk not managed	Probability	Impact	Rating	Controls to reduce risks
Loss of data due to insufficient back up	Irrecoverable loss of data. Recreation of database will require more time. Inaccurate results. Might have to repeat the study requiring more time and effort.	4	3	H	Daily back up of data on USB memory stick, laptop & mobile phone to minimize loss of data
Loss of data due to inappropriate, discriminatory or biased practices of social media platform Team e.g. Social media suddenly blocks user account	Same as before	4	3	H	Same as before
Undeclared Conflict of Interest	Could result in loss of confidence in research results. Negative publicity for the researcher.	4	4	H	PI ensured that any conflict of interest is declared. The present study has no conflict of interest. No funding was taken for the study.
Breach of Ethics, confidentiality	Negative publicity	4	4	E	PI has adequate ethics, good research practices and project management training. Ensured participants meet inclusion & exclusion study criteria. Informed consent was obtained. No personal info of participants was obtained. The Study was IRB exempt. Participants were encouraged to contact Principle Investigator if they have any questions. Participants were assigned codes.

Source: Author.

Table 11: Risk Register Continues

Risk	What can go wrong If risk not managed	Probability	Impact	Rating	Controls to reduce risks
Poor Quality of data.	The study will fail to achieve its objectives. Results may be unreportable / unpublishable.	4	4	H	To encourage detailed responses to open ended questions, E-survey was designed in MS word. This enhanced the quality of data collected. There is good evidence in literature that shows detailed responses are very likely when using a Word processor compared to pen and pencil Data quality was ensured by making sure that participants represent target population – PI confirmed responses with the study participants where it was necessary to do so. Data was digitised. Accompanying notes about the data were also entered on spreadsheet. Data was checked for completeness and for double entries. Manuscript was submitted to peer review journal to ensure good data quality
Fraud in data collection	Study results will be invalid. Results will be unpublishable If published, study will has to be retracted.	3	3	High	Accuracy in data collection was ensured i.e. An E-survey was designed and implemented by social media platform. PI has good research training.

Table 12: Risk Register Continues

Risk	What can go wrong If risk not managed	Probability	Impact	Rating	Controls to reduce risks
Poor Data analysis	Inaccurate study data will result in unpublishable results. If already published, study has to be retracted.	3	3	E	In order to remove nonsensical data entries following measures were taken: Descriptive data analysis was done to detect errors and to detect trends and get results. Data sorting was done i.e. data was grouped according to requirements The data was presented in multiple formats e.g. in Figures and Tables Filled survey was received via multiple channels i.e. via Social media platform and via email. Clear instructions given to the study participants on filling the questionnaire
Poor Data Authenticity	Actual results of the study could be changed.	3	5	E	It was ensured by preventing unauthorized access to data that may result to unauthorized changes in data. Only PI had access to Survey results and database on her Laptop and mobile. The laptop and mobile are password protected. Kept a single master file. Recorded all changes to master file/database

Table 13: Risk Register Continues

Risk	What can go wrong If risk not managed	Probability	Impact	Rating	Controls to reduce risks
Financial risks e.g. lack of money & funding	Study could not be completed on time, within budget or lack quality data. Study will need to be halted.	1	2	L	The risk was managed by minimizing financial costs of conducting the project e.g. participant recruitment and data collection was carried out electronically (E-survey). PI carried out data analysis, data collection and also designed E-questionnaire. Thus there was no postage and data entry costs. PI used her own laptop and mobile to design, implement E-survey and to collect and analyse data thereby saving time and money. Number of follow up contacts was not limited by the research budget.
Low Response rate	Difficult to generalize results				Reminders were sent to increase response rate. All respondents were working in major PBT centres. Respondents have working knowledge of PBT.

Each risk has two components i.e. i) Probability (likelihood) of an event/risk occurring and ii) Consequences (Impact) of an event/risk on project objectives. Risk analysis was carried out using method described in the Australian and New Zealand standard on Risk management, [22] and Risk Management Plan for Research on the Alfred Campus [23]. However the probability and impact scales were generated by the author

Stages in Risk Analysis

1. In current qualitative risk analysis, firstly two risk scales were created i.e. a risk's probability scale and ii) a risk's Impact scale. See Table **7**, **8**. These scales used ordinal values to represent probability and impact values e.g. Probability scale used ordinal values from Rare to Almost certain. PMBOK guide also mentions use of Probability and impact scales and use of ordinal as well as cardinal (numerical) values to describe likelihood of an event and impact of an event on project objectives [24].

2. Secondly a risk rating matrix or probability impact matrix was used as defined by Alfred Campus, Australia [23]. The source was modified.

3. Thirdly a risk register was generated that included probability, impact and risk rating values as well as other parameters.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found below:

Glossary

Adaptive Radiotherapy

It allows replanning of patient treatment based on either structural and spatial changes occurring over duration of treatment with the aim of decreasing overdosage of critical structures, enhancing dose homogeneity and preserving coverage of the target and/or replanning patient treatment based on response to the treatment with the aim of dose escalation to treat persistent disease and/or de-escalating dose to spare normal tissue.

Cyclotron

It is a particle accelerator that accelerates charged atomic or sub atomic (proton) particles in a circular path in the presence of constant magnetic field. The constant magnetic field is produced by dipole magnets. The oscillating electric field in gaps between electrodes accelerates the particles.

Distal Edge Tracking

This technique puts Bragg peaks on the distal edge of the target volume only and thus generates a highly non uniform dose per treatment field. The desired uniform dose is achieved by superimposing multiple fields from different directions.

Intensity Modulated Proton Therapy

It is a pencil beam scanning technique that gives dose modulation to optimally balance dose distributions to the target and various organs at risk. In IMPT modulation from combined dose distributions from all beams can be performed in three dimensions. It simultaneously optimizes fluences of all pencil beams from all fields, resulting in individual fields becoming in homogenous but the final dose across the target can be still homogeneous.

Linear Energy Transfer

The average energy deposited per unit length of track (KeV/μm).

Passive Scattering

It is a proton delivery technique. In passive scattering, a narrow proton pencil beam emerging from a cyclotron or synchrotron is scattered or spread out by a single or double scatterers to obtain uniform beam laterally. This is done to adequately treat the entire treatment volume.

Patch and through

This strategy is often utilized in passively scattered proton therapy to match the sharp distal edge of the spread out Bragg peak of the patch field to the lateral penumbra of the through field at 50% isodose line.

Pencil Beam Scanning

It is a proton delivery technique. In Pencil Beam scanning, the mono-energetic narrow proton pencil beam is magnetically scanned in x-y direction perpendicular to the beam direction across the target. The depth (z) scan is achieved by means of energy variation. The energy can be varied from spot to spot or continuously along the path. This method does not require a collimator and compensator and allows for intensity modulated proton therapy. Pencil beam scanning achieves both distal and proximal dose conformality.

Relative Biological Effectiveness

The Relative Biological Effectiveness is defined as the ratio of the doses required by two radiations to produce the same level of effect.

Single Field Uniform Dose

In Single Field Uniform dose pencil beam influences are optimized for each field independently and with the single goal of creating a dose distribution across the target that is as homogeneous as possible. Different field weights can be assigned to the multiple fields to adjust contribution of each field to the target volume.

Spot Scanning

It is a form of Pencil beam scanning that delivers proton beams spot by spot in a discrete manner. The technique was developed by NIRS, Japan in 1980. As the beam pass through the tumour, proton spots fill the thin thickness (0.7 to 1 sigma; Gaussian shape of spot size) of tumour at the depth where the Bragg peak is created. In spot scanning beam is paused while it moves from one voxel to another of target volume.

Surface Guided Radiotherapy

It uses optical image guidance to visually track patient's position on radiation therapy treatment couch for setup before and constant monitoring during radiation therapy treatment. It achieves this by matching the external surface of the patient with pre-treatment scans.

Synchrotron

it is a particle accelerator that consists of circular accelerator ring. The electromagnetic resonant cavities around the ring accelerate particles during each circulation. Synchrotron allow creation of proton beams with a range of energies.

Uniform Scanning

It is a proton delivery technique that utilizes magnets to scan a broad beam across a treatment field and entails the use of collimators to shape the beam (The other type of scanning is called Pencil beam scanning).

APPENDIX A: A SAMPLE E-QUESTIONNAIRE

A Survey of Proton Therapy

This survey identifies the education/training level for Proton Therapy Radiation treatment planning and delivery. It is a mainly multiple choice questionnaire and I would greatly appreciate if you could take time to complete it. Please select your responses by choosing from given options and typing it in the space provided after each question (e.g. to answer Q1 you may chose to type **B** if you are Radiotherapy manager). Please return the completed survey to: Auj-E Taqaddas (Principal Investigator) email:taqaddas2018@gmail.com by 12th Dec 2019

Demographic Information:

Q.1. In what role you are employed?

- A. Proton Therapy Medical Physicist.
- B. Radiotherapy Manager
- C. Radiation Treatment Planning Head/manager
- D. Training Manager
- E. Dosimetrist
- F. Radiographer
- G. Treatment planning Physicist
- H. Research Physicist
- I. Medical Physics Head
- J. Trainee Medical Physicist
- K. Medical physics assistant
- L. Other (Please specify)

Q.2. Do you have working knowledge or only theoretical knowledge of protons and proton therapy?

Q.3. Do you work in a Proton therapy centre or hospital?

Q.4. What is the geographical location of your hospital?

District/Province /City /Country

Education and Training

Q.5. Do you use any of the following technologies? Please select all those applications that you use in your department to treat cancer patients

- A. IMPT (Intensity modulated Proton Therapy)
- B. Single Field Uniform Scanning
- C. Single Field Uniform Dose
- D. Patch and through field
- E. Distal Edge Tracking
- F. IGRT (Image Guided Radiation therapy)guided Proton therapy
- G. Adaptive Proton Therapy
- H. Passive Scattering
- I. Spot Scanning
- J. Other (Please specify):

Q6 Which IGRT system or technique you use in proton therapy treatment planning and delivery (e.g. Cone beam CT; Integrated MRI,)?

Q.7 Which Adaptive Radiation therapy system or technique you use?

Q. 8 Which proton treatment planning system you use in your department?

Q.9 Which body sites you use for proton therapy treatment ? please write your choice/s

- A. Brain cancers,
- B. head and neck cancers ,
- C. Eye tumours,
- D. CNS tumours,
- E. Prostate cancer;
- F. Gynecological tumours,
- G. abdominal tumours,
- H. sarcomas of limbs,
- I. Others (Please specify)

Q.10. Do you have staff with Proton treatment planning skills?

- A. Yes
- B. No

Q. 11. If answering yes to the Question 10 where did they get their training?

- A. In-house training
- B. Proton Treatment planning system manufacturers (e.g. Philips oncology systems, etc.)
- C. University
- D. College
- E. Others (Please specify)

Q. 12. Do you have staff with Proton therapy Commissioning and QA skills and experience?

- A. Yes
- B. No

Q. 13. If answering yes to question 12 where did they get their training?

- A. In-house training
- B. Proton therapy Treatment Planning System manufacturers (e.g. Philips, RayStation etc.)
- C. University
- D. College
- E. Others (Please specify)

(You can type your answer here)

Q.14. In your view what Proton therapy (PT) skills are required now?

- A. Proton therapy Commissioning
- B. PT QA
- C. PT Radiation Treatment Planning
- D. PT Dose verification
- E. Other (Please specify)

(Please Type your answer here)

Q.15. In your view what Proton therapy skills are required in next 5 years?

- A. PT Commissioning
- B. PT QA
- C. PT Treatment Planning
- D. PT Dose verification
- E. Other

Q.16. How do you think the education and training for Proton therapy can be improved? (Please Type your answer here).

Q.17. In your opinion which Proton therapy planning techniques (e.g. conformal PT, Uniform Scanning, IMPT) are better than photon 3D conformal planning, Photon VMAT (Volumetric modulated Arc therapy) and Photon IMRT and for which body sites?

Proton treatment planning technique/s that is better than

Photon 3D CRT

thoracic

Photon VMAT

Body site

Photon IMRT

Body site

Q.18. What improvements you would like to see in your current Proton treatment planning system (TPS)?

Q.19. What improvements you would like to see in your current Proton treatment delivery and imaging System?

Q.20. What Proton treatment delivery system do you use (e.g. IBA cyclotrons, Synchrotron, ProBeam)?

Quality Assurance and Dosimetry

Q.21. What patient specific Quality Assurance tests you use on daily and weekly basis to ensure accuracy of proton therapy treatment delivery?

Daily
Weekly

Q.22. How do you assure Proton therapy treatment plan verification?

Q.23. Which equipment or device you use to verify treatment plan and dose (e.g. Delta4 phantom)?

A. 2D dose verification system
B. 3D dose verification system
C. In vivo dose verification
D. Volumetric in room verification tools

Radiation safety

Q. 24. What qualifications and/experience is required to work in Proton radiation safety in your country and institute (hospital)?

Thank you again for answering these questions.

APPENDIX B: LIST OF PBT FACILITIES

	LIST OF FACILITIES WHOSE PROFESSIONALS PARTICIPATED IN THE SURVEY	NUMBER OF PROFESSIONALS WHO PARTICIPATED IN THE SURVEY FROM EACH FACILITY
1	Miami Cancer Institute, Florida	1
2	Beaumont Proton Therapy Centre, Royal Oak, Michigan	1
3	MD Anderson Cancer Centre, Houston, Texas	2
4	Texas Centre for Proton Therapy, Irving, Texas	1
5	Massachusetts General Hospital, Boston, Massachusetts	2
6	University Hospital (UH) Proton therapy centre, Cleveland, Ohio	1
7	University of Cincinnati Medical Centre Proton Therapy Centre, Cincinnati, Ohio	1
8	Provision CARES Proton Therapy Centre, Knoxville, Tennessee	2
9	Northwestern Medicine Proton Centre, Warrenville, Illinois and Procure PTC Somerset, New Jersey.	1
10	Northwestern Medicine Centre, Warrenville, Illinois (Chicago suburbs)	1
11	Riverside Health System, Newport News, Virginia	1
12	Seattle Cancer Care Alliance Proton Therapy Centre, Seattle, Washington	1

APPENDIX C: ABBREVIATIONS

ART = Adaptive Radiotherapy

CBCT = Cone Beam CT

CNS = Central Nervous System

CT = Computerised Tomography

DET	=	Digital Edge Tracking
DIBH	=	Deep Inspiration Breath Hold
DS	=	Double scattering
FL	=	Florida
HNC	=	Head and Neck cancer
IGRT	=	Image Guided Radiotherapy
IL	=	Illinois
IS	=	Imaging system
IMPT	=	Intensity Modulated Proton Therapy
KV	=	Kilovoltage
LET	=	Linear Energy Transfer
MA	=	Massachusetts
MI	=	Michigan
NJ	=	New Jersey
OAR	=	Organs at risk
OBL	=	Oblique
OH	=	Ohio
PBS	=	Pencil beam scanning
PBT	=	Proton Beam Therapy
PEG	=	Percutaneous endoscopic gastrostomy
POST	=	Posterior
PS	=	Passive scattering
PTF	=	Patch and through field
QA	=	Quality Assurance
RBE	=	Relative Biological Effectiveness
RTT	=	Radiation Therapy Technologist
SC	=	Spot scanning
SFUD	=	Single field uniform dose
SIB	=	Simultaneous integrated boost
SOBP	=	Spread out Bragg peak

SWOT	=	Strengths, Weaknesses, Opportunities, Threats
TX	=	Texas
TN	=	Tennessee
TPS	=	Treatment Planning System
Uni	=	University
US	=	Uniform scanning
VA	=	Virginia
VMAT	=	Volumetric Modulated Arc Therapy
WA	=	Washington
USA	=	United States of America

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