PROTON AND CARBON LINACS FOR HADRON THERAPY

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Abstract

Beams of 200 MeV protons and 400 MeV/u fully stripped carbon ions are used for the treatment of solid tumours seated at a maximum depth of 27 cm. More than 100'000 patients have been treated with proton beams and more than 10'000 with carbon ions. Very low proton currents - of the order of 1 nA - are enough to deliver the typical dose of 2 Gy/l in one minute. In the case of carbon ions the currents are of the order of 0.1-0.2 nA. For this reason 3 GHz linacs are well suited in spite of the small apertures and low duty cycle. The main advantage of linacs, pulsing at 200-400 Hz, is that the output energy can be continuously varied pulse-by-pulse and in 2-3 min a moving tumour target can be covered about 10 times by deposing the dose in many thousands of 'spots'.

High frequency hadron therapy linacs have been studied in the last 20 years and are now being built as hearts of proton therapy centres, while carbon ion linacs are still in the designing stage. At present the main challenges are the reduction of the footprint of compact 'single-room' proton machines and the power efficiency of dual proton and carbon ions 'multi-room' facilities.

INTRODUCTION

In developed countries more than 2'000 patients every 1 million inhabitants are subject to radiation therapy every year [1]. In more than 95% of cases, the treatment of the tumour disease consists in irradiation with X-rays. Hadron therapy has developed in the last 60 years as an advanced technique in radiation therapy that allows a not invasive and precise irradiation of solid tumours with the advantage of sparing the surrounding healthy tissues. The proposal, published in 1946 by 'Bob' Wilson [2], was based on the presence of the Bragg peak in the depth-dose profile of charged hadrons.

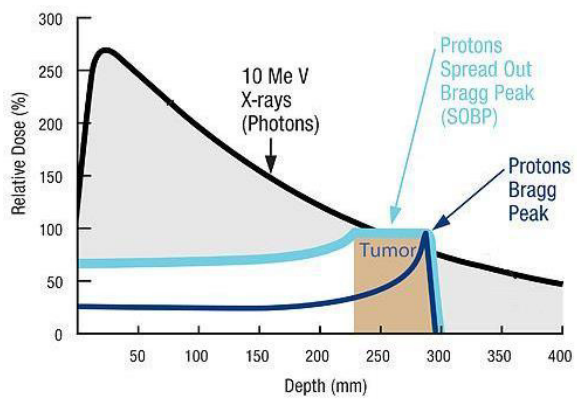

Figure 1: Comparison of depth-dose profile for X-rays (black) and charged hadrons (blue).

The energy released by a beam of mono-energetic charged hadrons is concentrated at the end of the range in matter. Since by changing the beam energy one can adjust the depth of the Bragg peak, the overlapping of many Bragg peaks produces a flat dose distribution in the tumour region, as seen in Fig. 1. The same figure shows that most of the energy deposited by an X-ray beam is outside of the tumour target so that, even with many crossed beams, in an X-ray-treatment, healthy normal tissues are in a 'bath' of radiation, while the total energy delivered to normal tissues with charged hadrons is typically a factor 3-4 smaller than with X-rays.

The use of linacs for hadron therapy has been proposed in the late eighties. Since 1993, TERA Foundation, in parallel with the study of a synchrotron based dual facility for the Italian hadrontherapy project - concluded with the construction of CNAO in Pavia [3] - initiated the study of high frequency linacs for hadron therapy applications. In 2009 a review of the subject was published by Reviews of Accelerator Science and Technology [4].

THE BEGINNINGS

Conventional X-ray Therapy

In the world more than 20'000 electron linacs are used by radiation oncologists daily; they represent 50% of all the existing accelerators having energy larger than 1 MeV [5]. Most of the linacs are based on normal conducting structures at 3 GHz; they are powered by a single magnetron or klystron and are mounted on a rotating support (gantry). The electron beam energy is in the typical range 6-20 MeV.

The Linac Approach to Proton Therapy

The use of linac for protons has first been proposed in 1991 [6]. The system was made up of an RFQ–DTL operating at 499.5 MHz, followed by a 3 GHz Cell Coupled Linac (CCL) that accelerated protons from 70 to 250 MeV (Fig. 2). The energy modulation could be achieved by switching off the modules and by using degrading absorbers.

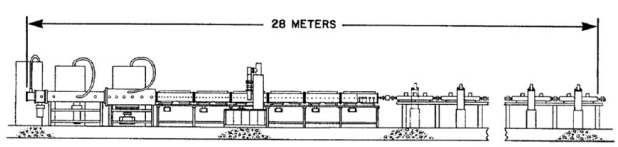

Figure 2: Schematic layout of the model PL-250 proton therapy linac designed by R. Hamm, K. Crandall and J. Potter [6].

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This type of solution based on RFQ, DTL and CCL has been named “all linac” approach.

In the so-called “cyclinac” approach the facility is a combination of a high intensity low energy cyclotron, which pre-accelerates the protons up to 25-35 MeV, and a linear CCL booster that accelerates the beam up to 200-230 MeV. In this approach all the accelerating units have the same CCL structure; three different linacs are instead needed for the all-linac solution. Moreover, the cyclotron can also produce, by night and during the weekends, medical radioisotopes not accessible to the hospital baby cyclotrons, which reach at maximum 19 MeV.

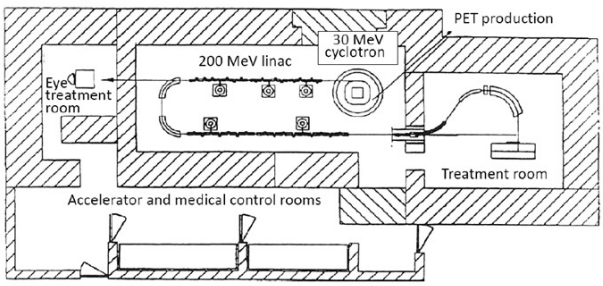

Figure 3: Schematic layout of the first “cyclinac” approach to proton therapy proposed in 1994 by one of the authors [7].

THE RATIONALE FOR PROTON AND CARBON ION TUMOUR THERAPY

X-rays have two main problems: i) they irradiate unwanted close-by ‘critical’ organs, as shown in Fig. 1, and ii) they cannot cure ‘radioresistant’ tumours (about 5% of the total), i.e. tumours that are less sensitive to radiation than the surrounding normal tissues.

Charged hadrons are a valuable tool in radiotherapy because, firstly, they spare healthy normal tissues (by reducing the dose delivered in the entrance channel and by not delivering any dose in the exit channel). Secondly, carbon ions have the capability of better controlling ‘radioresistant’ tumour because – due to the six times larger charge than protons – they have a higher radiobiological efficiency (RBE). Indeed, carbon ions produce along the track 25 times more ionizations than protons of the same range, causing – when they traverse a cell nucleus – a great number of *clustered* unrepairable ‘double strand breaks’. This is at the basis of their higher efficiency in killing radioresistant tumour cells.

LIBO, THE FIRST LINAC BOOSTER

Under the leadership of Mario Weiss, TERA - in collaboration with CERN and the INFN Sections of Milano and Naples - built and tested with protons LIBO (*LInac BOoster*), the 3 GHz *Cell Coupled Linac* (CCL) of Figs. 4 and 5. This accelerating Unit was made of 4 ‘tanks’, in which the average accelerating field was E_0 = 16 MV/m.

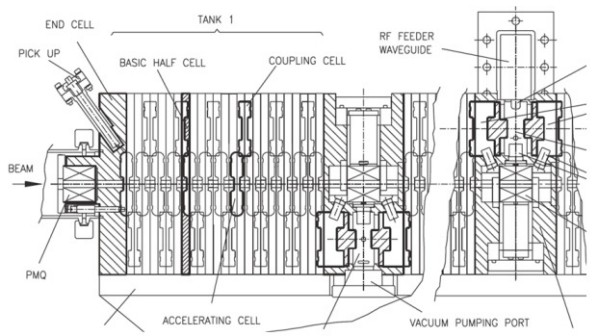

Figure 4: In this drawing of LIBO an accelerating cell and a coupling cell are highlighted in black.

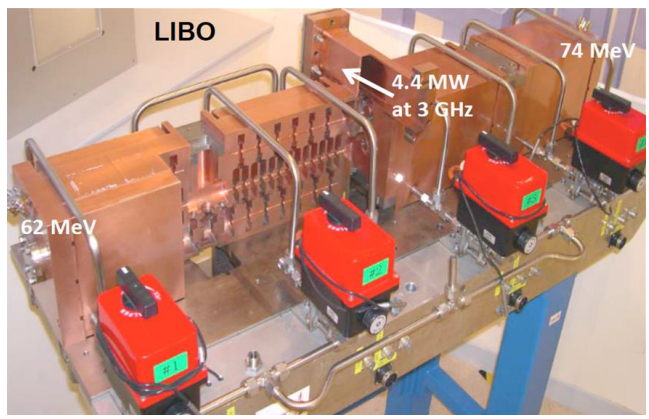

Figure 5: Cut-away of LIBO.

The design of LIBO and the results of the acceleration test - which completely correspond to beam dynamics calculations - are summarized in Refs. [8, 9].

A linac is made of about ten ‘Units’ similar to the one of Fig. 5. To explain the advantages of such a therapy linac one has to recall that the accelerators used in hadron therapy are either (synchro)cyclotrons or synchrotrons. Most of the 42 proton centres in operation [10] are equipped with cyclotrons while for carbon therapy only synchrotrons are used.

Normal cyclotrons are compact (with a typical diameter of about 2.5 meters) and are CW machines, so that the beam (pulsed at 50-100 MHz) is always present during a patient irradiation. On the other hand, the beam energy can only be varied by passive means, i.e. with motors that introduce in the beam absorbers of various thicknesses. The time needed for an energy change is of the order of 50-100 ms. Synchrotrons are more complex and larger in size than cyclotrons (with typical diameter of 7-8 m for proton synchrotrons and 20-25 m for carbon ions machines). The beam is extracted in spills of a couple of seconds with a time separation of 1-2 s and the energy can be varied actively, by adjusting the number of turns in the machine.

If a linac running at 200 Hz is composed of a large number of accelerating units (typically 10), singly powered by *independently* controlled klystrons, the final beam energy can be varied *continuously* from pulse to pulse, i.e. every 5 ms, by adjusting the amplitude and/or

phase of the klystron signals [4]. This feature makes possible the implementation of the active *spot scanning technique* with tumour *multi-painting*, the best possible way for treating moving organs [11,12]. This is a unique feature of all linacs discussed in this paper.

THE PRESENT: "LIGHT" BY A.D.A.M.

In 2007, to transform LIBO in a commercial product, Alberto Colussi - an Italian-Suisse entrepreneur - created A.D.A.M., a CERN spin-off company. Since then the laboratories of A.D.A.M. are on CERN premises. In 2013 the UK company Advanced Oncotherapy (AVO) acquired A.D.A.M..

A.D.A.M. has been developing a linac for proton therapy, based on the TERA design of LIBO (Figs. 4 and 5). A Unit of LIGHT (*Linac for Image Guided Hadron Therapy*), which accelerates protons from 30 MeV to 41 MeV, has been power tested with a 7.5 MW modulator/klystron system (Fig. 6).

Figure 6: First Unit of LIGHT built and tested by A.D.A.M..

LIGHT differs from LIBO mainly for the open space in which the Permanent Magnet Quadrupoles (PMQs), which focus the accelerated beam, are inserted.

By combining the 5 MeV 750 MHz RFQ built by CERN [13] with the low-beta Side Coupled Drift Tube Linac (SCDTL) by ENEA and the CCL of Figure 6, A.D.A.M. is building on CERN premises the section of LIGHT (Fig. 7) that accelerates proton up to 100 MeV.

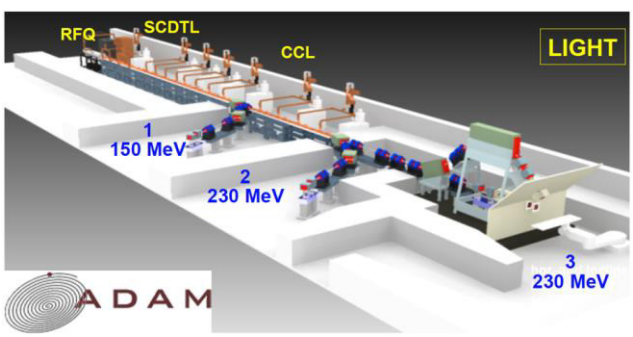

Figure 7: Layout of LIGHT, which is composed of three linear accelerators: RFQ (up to 5 MeV), SCDTL (up to 35 MeV) and CCL up to 230 MeV.

After the acceleration tests, the first section of LIGHT will be mounted in a hospital followed by the CCL that accelerates protons from 100 MeV up to 230 MeV. Figure 7 shows the complete layout that features four fixed beam lines serving three treatment rooms.

THE PRESENT: "IMPLART" BY ENEA

The ENEA group of Luigi Picardi and Concetta Ronsivalle has proposed and built a Side Coupled Drift Tube Linac (SCDTL) which – because of the larger impedance - is better suited than a CCL to accelerate protons from a few MeV to 40-70 MeV [14,15,16].

As shown in Fig. 7, an SCDTL - made of a series of DTL cells that are side coupled one to the next (Fig. 8) - will be the second stage of LIGHT built by A.D.A.M. at CERN.

Figure 8: The SCDTL structure mounted in the ENEA laboratories at Frascati.

In the Frascati ENEA laboratories the first SCDTL has accelerated a proton beam – produced by a commercial RFQ-DTL system – from 7 MeV to 11.7 MeV. This is the first section of the *Intensity Modulated Proton Linear Accelerator for Radio Therapy* (IMPLART) of Fig 9.

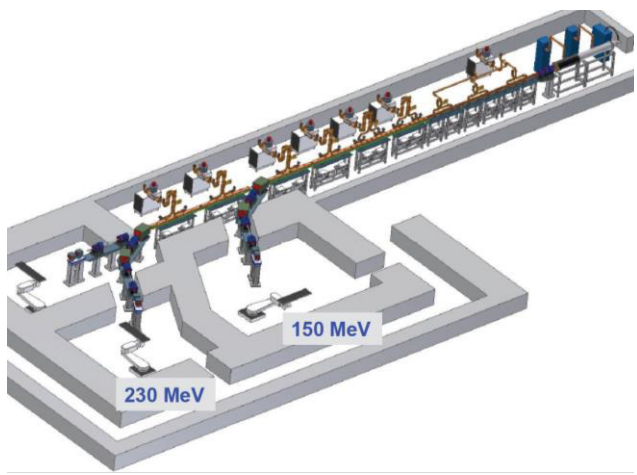

Figure 9: Layout of IMPLART by ENEA.

Public funds have been allocated to reach 150 MeV and to transport the facility to the IFO hospital in Rome.

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STUDIES FOR THE FUTURE: HIGH-GRADIENT HADRON STRUCTURES

With respect to X-ray linacs hadron therapy linacs have to overcome two main challenges. Firstly, the speed β of the particles varies in the range 0.1-0.6 and the accelerating structures are characterized by maximum surface electric fields E_s on the typical 'nose' cones (Fig.10) that – for the *same* average accelerating gradient – are twice larger than the ones of a $\beta = 1$ linac. Indeed, the typical ratio between E_s and the average gradient E_0 is E_s/E_0=4-5 for hadron structures and 2 for electron structures.

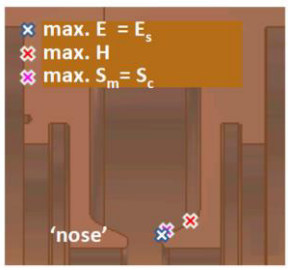

Figure 10: In a hadron linac the maximum surface electric field is close to the point of the nose.

Secondly, while the maximum energy of an X-ray linac is 20 MeV, the proton beam needs to be accelerated up to 200-230 MeV in a reasonable distance. This requires larger gradients and thus possibly dangerous Break-Down Rates (BDR), which are rapidly varying functions of E_s.

TERA Foundation, in collaboration with the CLIC RF structure development group led by W. Wuensch, has performed extensive studies on high gradient accelerating structures for applications in hadron therapy [17]. Two single cell standing wave accelerating structures, one at 3.0 GHz and one at 5.7 GHz, have been designed, built and high power tested. Measurements of the performance in terms of BDR were conducted and compared with the results of single cell standing wave X-band accelerating cavities tested at SLAC (Fig. 11).

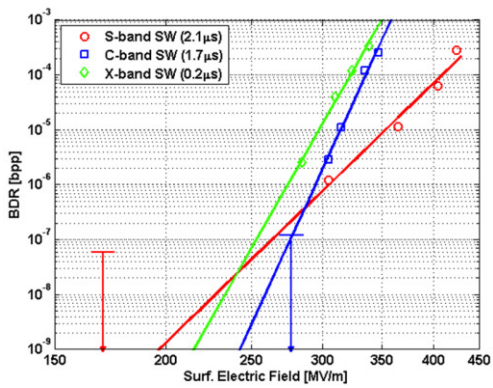

Figure 11: Comparison of results of BDR measurements performed at different frequencies [18].

From these results it has been concluded that the maximum modified Poynting vector S_c – introduced in [19] – describes the BDR measurements in the 3-12 GHz frequency range better than the maximum surface electric field E_s. This is the quantitative basis of the applications described in the last two Sections.

THE FUTURE HIGH-GRADIENT LINAC: "TULIP"

The about 45 proton therapy centres running in the world are 'multi-room' facilities in the sense that one accelerator feeds typically three treatment rooms. This approach makes good use of the accelerator but requires long displacements of many patients because the facility serves more than 5 million people. Many experts are convinced that 'single-room' serving 1.5 million people will have a place in the future development of hadron therapy. Since a couple of years two companies (IBA and MeVion) offer cyclotron based single room facilities.

The project TULIP (*Turning LInac for Protontherapy*), patented by TERA, foresees a linac mounted on a rotating gantry used as a booster for protons previously accelerated by a cyclotron [20]. In the tanks the maximum average gradient is E_0 = 30 MV/m.

As it is shown in Fig. 12, the RF power transmission is made possible by high power rotating joints developed in collaboration with the CLIC group.

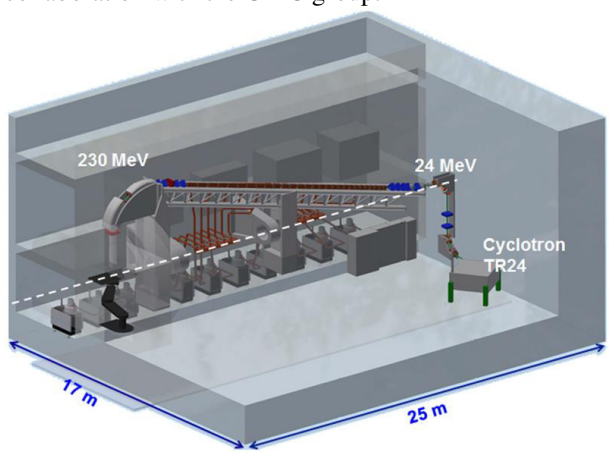

Figure 12: First design of the 11 m long TULIP; the injector is a 24 MeV commercial cyclotron.

TULIP 2.0 of Fig. 13 is based a novel structure of the Backward Travelling Wave (BTW) type [21].

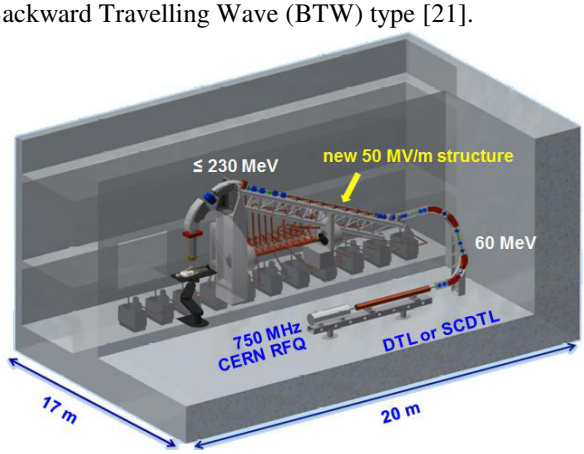

Figure 13: TULIP 2, based on a BTW linac, is 6 m long.

This new 50 MV/m design will also include a novel injector based on the novel high frequency RFQ under construction at CERN [13], followed by an SCDTL section.

THE FUTURE HIGH-EFFICIENCY LINAC: "CABOTO"

The most recent developments are related to the increase in power efficiency of the whole system. This is crucial for a carbon ion facility based on a linac, such as the CABOTO (*CArbon BOoster for Therapy in Oncology*) design proposed and patented by TERA Foundation [22].

Figure 14 shows the schematic layout of a cyclinac based carbon ion facility. The cyclotron can be similar to the one built by VECC in Kolkata (Fig. 15), which accelerates light Q/A = 1/2 ions up to 80 MeV/u.

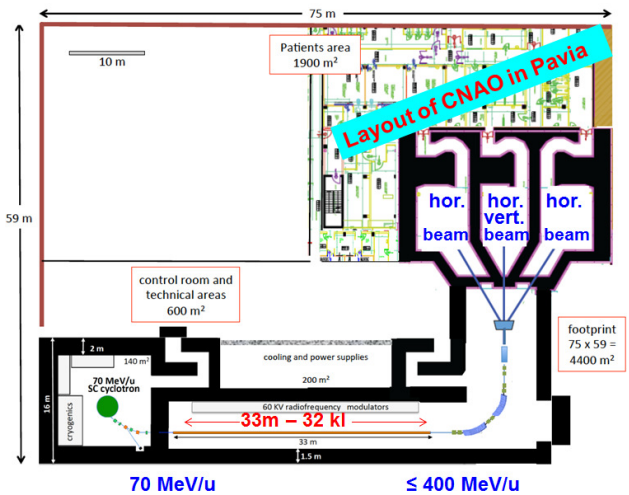

Figure 14: Preliminary layout of the linac based carbon ion facility based on high efficiency design.

The 33 m long 300-400 Hz linac will boost fully stripped carbon ions from 70 MeV/u to 400 MeV/u. In this case, the voltage gain of the particles is very large: (400-70) x 2 = 660 MeV. Using very high gradients, such as the ones foreseen for TULIP, would bring the overall power consumption to unacceptable levels. The new linac (Fig. 15) is thus running at 30 MV/m.

Figure 15: The Indian Variable Energy Cyclotron weighs about 100 tons [23].

To reduce the power it is foreseen to power the 32 CCL units with 32 multi-beam 7 MW klystrons (MBK) having 60% efficiency, which will run at 300-400 Hz with 3.5 μs RF pulses (duty cycle = 1-1.5 10^{-3}). Similar klystrons, which are the object of a CERN tender launched by the CLIC group, need only 60 kV so that the modulators are oil-free and small. The objective is to run the accelerator complex with a plug-power not larger than 1.2 MW.

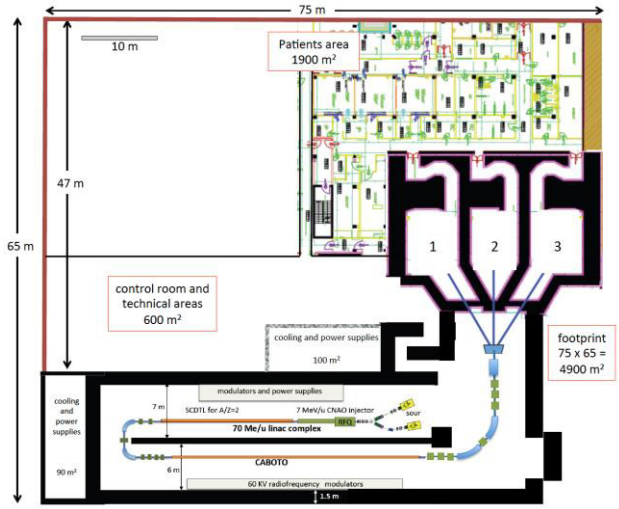

Figure 16: Preliminary layout of the all-linac carbon ion facility based on high efficiency design.

In the layouts of Figs. 14 and 16 the three treatment rooms and the distribution of the close-by rooms are copied from CNAO in Pavia [3]. The footprints of the accelerators and the power supplies of the two versions of CABOTO are 750 m^2 and 1000 m^2, to be compared with the 1600 m^2 of CNAO.

CONCLUSIONS

The first CCL accelerating Unit LIBO accelerated protons in the early 2000s demonstrating the feasibility of such machines, which run at 200-400 Hz and have the unique feature that the energy can be changed every pulse. To make use of this property the currents in the magnets of the transport lines have to be adjusted every few milliseconds. The group of D. Tommasini at CERN and TERA are constructing, with funds of the CERN Knowledge Transfer (KT) group, a prototype.

A commercial product has been developed by the CERN spin-off company A.D.A.M. based on an all-linear approach that includes a newly developed 750 MHz RFQ, a SCDTL section and a CCL section based on the TERA design. A similar system is being built in Frascati by ENEA.

Novel designs aiming at high gradients and high efficiency linacs for proton single-room facilities and carbon ion multi-room facilities are under study by TERA in collaboration with the CLIC group and with the support of CERN KT group.

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REFERENCES

[1] *Carbon ion therapy*, Radiotherapy and Oncology 73/2 (2004) 1

[2] R. R. Wilson, *Radiological use of fast protons*, Radiology, 47:487–491, 1946

[3] S. Rossi, *The status of CNAO*, Eur. Phys. J. Plus (2011) 126:78

[4] U. Amaldi, S. Braccini, and P. Puggioni, *High frequency linacs for hadrontherapy*, Reviews of Accelerator Science and Technology RAST02: 111-131, 2009

[5] W. Maciszewski and W. Scharf, *Particle Accelerators for Radiotherapy*, Int. J. of Radiation Oncology, 2004

[6] R. W. Hamm, K. R. Crandall and J. M. Potter, *Preliminary design of a dedicated proton therapy linac*, PAC'91, San Francisco, May 1991

[7] U. Amaldi, *The Italian hadrontherapy project, in Hadron Therapy in Oncology*, eds. U. Amaldi and B. Larsson (Elsevier, 1994), p.45

[8] U. Amaldi et al., *LIBO a linac-booster for protontherapy: construction and test of a prototype*, NIM A, 521:512–529, 2004

[9] C. De Martinis et al., *Acceleration tests of a 3 GHz proton linear accelerator (LIBO) for hadrontherapy*, NIM A, 681:10–15, 2012

[10] Particle Therapy Co-Operative Group website, http://www.ptcog.ch/index.php/facilities-in-operation

[11] E. Pedroni et al., *The 200-MeV proton therapy project at the Paul Scherrer Institute: Conceptual design and practical realization*, Med. Phys. 22 (1995) 37

[12] C. Bert et al., *Target motion tracking with a scanned particle beam*, Medical Physics, 34:4768–4771, 2007

[13] M. Vretenar, *A compact high-frequency RFQ for medical applications*, LINAC'14, Geneva, September 2014, these proceedings

[14] L. Picardi, C. Ronsivalle, *The first module of the 3 GHz Side Coupled Drift Tube Linac (SCDTL)*, EPAC 2000, Vienna, June 2000

[15] L. Picardi, *High power RF tests of the First Module of the Top Linac SCDTL Structure*, EPAC'06, Edinburgh, June 2006

[16] L. Picardi et al., *Accelerating a cyclotron 18MeV Proton Beam by a SCDTL Linac*, PAC'09, Vancouver, May 2009

[17] A. Degiovanni et al., *TERA high gradient test program of RF cavities for medical linear accelerators*, NIM A, 657(1):55-58, 2011

[18] A. Degiovanni, *High Gradient Proton Linacs For Medical Applications*, EPFL Thesis 6069, 2014

[19] A. Grudiev, S. Calatroni, and W. Wuensch, *A new local field quantity describing the high gradient limit of accelerating structures*, Phys. Rev. ST Accel. Beams, 12, 102001:1–11, 2009

[20] A. Degiovanni et al., *Design of a fast-cycling high-gradient rotating linac for protontherapy*, IPAC'13, Shanghai, May 2013

[21] S. Benedetti et al., *RF Design of a Novel S-Band Backward Traveling Wave Linac for Proton Therapy*, LINAC'14, Geneva, September 2014, these proceedings

[22] U. Amaldi, M. Crescenti, R. Zennaro, *Ion acceleration system for hadrontherapy*, Patent US 7423278

[23] R. K. Bhandari, *Status of the Kolkata K500 Superconducting Cyclotron*, CYC'04, Tokyo, October 2004