

## SHORT COMMUNICATION

Mini tandem accelerator-based neutron or  
gamma-ray generator for radiotherapyKa-Ngo Leung<sup>1,2\*</sup>  and James K. Leung<sup>2</sup><sup>1</sup>Department of Nuclear Engineering, University of California, Berkeley, California, United States of America<sup>2</sup>Berkion Technology LLC, Berkeley, California, United States of America**Abstract**

A miniature tandem accelerator is being developed to operate as a neutron or gamma-ray tube for radiotherapy applications. This new tool is operated with a high-frequency alternating current 1 mega-volt (MV) high-voltage pulser and a plasma-less H<sup>-</sup>/D<sup>-</sup> ion source, making it suitable to generate a high flux of fast or epithermal neutrons or high-energy gamma rays through the d-<sup>7</sup>Li, p-<sup>7</sup>Li or p-<sup>19</sup>F nuclear reactions. With the proper design, these mini tandem accelerator tubes can be modified for neutron, gamma-ray, or boron neutron capture therapy brachytherapy applications. By increasing the stripper foil voltage higher than 10 MV, proton brachytherapy can be performed for the treatment of small cancer tumors without the use of large and expensive high-energy accelerator systems.

**Keywords:** Tandem accelerator; Fast-neutron; Epithermal neutron; Gamma ray; Proton therapy; Brachytherapy; Boron neutron capture therapy

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**1. Introduction**

Electrostatic tandem accelerators are commonly used in mass spectrometry, material analysis, and radiocarbon dating.<sup>1</sup> In this type of accelerator system, negative hydrogen (H<sup>-</sup>) or deuterium (D<sup>-</sup>) ions are initially produced at ground potential. They are accelerated to a thin carbon foil, which is biased at a positive potential (V). Electrons of these negative ions are stripped off in passing through the carbon foil, forming positive hydrogen (H<sup>+</sup>) or deuterium (D<sup>+</sup>) ions. These H<sup>+</sup>/D<sup>+</sup> ions are accelerated toward the target electrode, which is at ground potential. As a result, the total energy gained by these ions will become 2 eV, where e is the electronic charge. There are several advantages in using the tandem-type accelerator for neutron or gamma ray production. First, one can double the interaction energy at the beam target, thereby greatly enhancing the neutron or gamma yield. Second, the target electrode is biased at ground potential while the high-voltage carbon foil is located at the center of the neutron/gamma tube. This arrangement will enable the high-voltage terminal to be located external to and away from the patient's body during cancer treatment. Fast neutron therapy, boron neutron capture therapy (BNCT), as well as different types of brachytherapy, can be performed with the mini tandem accelerator-based neutron/gamma generator described here.

## 2. Methods and design principle of the mini tandem accelerator

Recent experimental results have demonstrated that a substantial amount of H<sup>+</sup>/D<sup>+</sup> ions can be produced by thermal desorption processes.<sup>2</sup> In view of these new findings, short pulses of high-intensity neutron/gamma-ray beams can be formed by using nuclear reactions (such as d-d, d-<sup>10</sup>B, d-<sup>7</sup>Li, p-<sup>7</sup>Li or p-<sup>19</sup>F reactions) with the availability of a high-frequency alternating current (AC) high-voltage supply.<sup>3</sup> These “plasma-less” neutron/gamma tubes, like X-ray tubes, are very small in size. Using the tandem accelerator arrangement, the axial-type neutron or gamma tubes can be greatly improved for cancer treatment. Small-diameter neutron or gamma tubes can be designed for internal brachytherapy applications.

Figure 1 is a schematic diagram of a mini tandem accelerator operated as a neutron or gamma tube. The H<sup>+</sup>/D<sup>+</sup> ions are first formed by thermal emission from the emitter (which is at ground potential). They then accelerate toward the carbon foil, which is biased at 1 mega-volt (MV). With a thickness of 3 μg/cm<sup>2</sup>, the electrons of the H<sup>+</sup>/D<sup>+</sup> ions will be stripped by the foil to form H<sup>+</sup>/D<sup>+</sup> ions.<sup>4</sup> The positive H<sup>+</sup>/D<sup>+</sup> ions will be accelerated to the target electrode, which is at ground potential. As a result, the final

energy of the H<sup>+</sup>/D<sup>+</sup> ions will become 2 MeV. Depending on the reaction selected, a high flux of neutrons or gamma photons can be formed at the target. Table 1 summarizes the neutron/gamma rays produced for different nuclear reactions and their yield when the interaction energy is 2 MeV. Secondary emission electrons can also be created at the target and are accelerated back toward the carbon foil. To minimize these back-streaming electrons, a pair of permanent magnets is installed near the target electrode. The magnetic field generated by these magnets will suppress the secondary electrons from streaming back to the positively biased carbon foil. A prototype of the mini tandem accelerator-based neutron or gamma generator is shown in Figure 2. The dimension of this mini tandem accelerator is 6 cm × 20 cm (diameter × length).

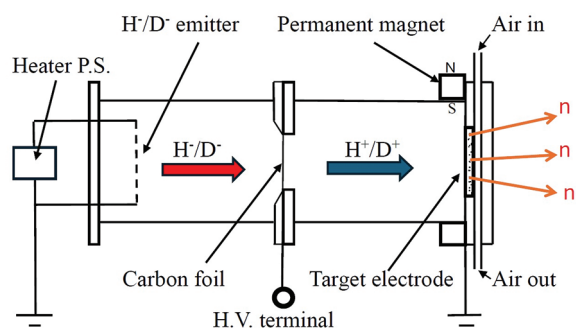
## 3. Results and discussion

### 3.1. Application of the mini tandem accelerator-based neutron/gamma tube in cancer therapy

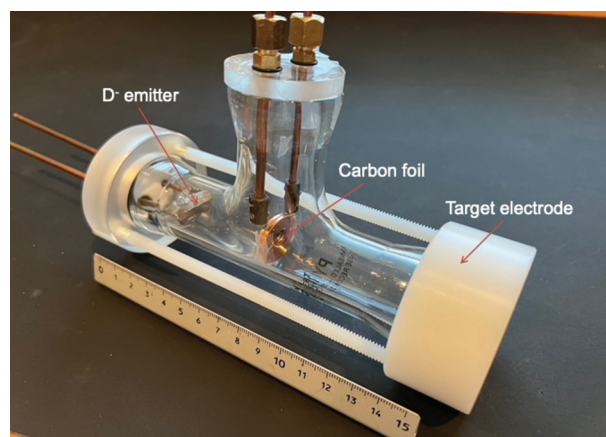
For fast neutron therapy, d-d, d-<sup>10</sup>B, or d-<sup>7</sup>Li neutron beams can be employed. When using an external beam, the d-<sup>7</sup>Li reaction is the better choice because it has the highest neutron yield and energy (Table 1). For a 1-cm-diameter D<sup>+</sup> beam, the beam current is approximately 2.5 mA. The thick target d-<sup>7</sup>Li neutron yield is 3.8 × 10<sup>12</sup> n/s. For 1% duty factor pulsed operation, the neutron yield becomes 3.8 × 10<sup>10</sup> n/s. Since the mini neutron tube can be positioned right next to the patient’s body, the neutron flux at the tumor is substantially high. The two major cell killing mechanisms of fast neutrons are the recoiled protons from its elastic collision with water molecules and the protons produced in the <sup>14</sup>N(n,p) reaction.<sup>5</sup> Due to the short range and high linear energy transfer, the protons leave a track with many free radicals in a small volume. These free radicals will react with biological molecules and may cause the death of these cells.<sup>5</sup>

**Table 1. Neutron/Gamma-ray produced by various nuclear reactions at 2 MeV interaction energy**

| Nuclear reaction                             | Energy of n/γ produced | Thick-target n/γ yield      |
|--|------------------------|-----------------------------|
| d-d  | 2.5 MeV neutrons       | 6.5×10 <sup>10</sup> n/mA/s |
| d- <sup>10</sup> B                           | 6 MeV neutrons         | 3×10 <sup>11</sup> n/mA/s   |
| d- <sup>7</sup> Li                           | 10, 13 MeV neutrons    | 1.5×10 <sup>12</sup> n/mA/s |
| p- <sup>7</sup> Li (E <sub>p</sub> =1.9 MeV) | Epithermal neutrons    | 1.5×10 <sup>10</sup> n/mA/s |
| p- <sup>19</sup> F                           | 6 MeV gammas           | 6×10 <sup>10</sup> γ/mA/s   |
| p- <sup>7</sup> Li (E <sub>p</sub> =1.8 MeV) | 480 keV gammas         | 2×10 <sup>11</sup> γ/mA/s   |



**Figure 1.** Schematic of a tandem accelerator-based neutron generator. Schematic created by the authors. Abbreviations: H.V.: High-voltage; P.S.: Power supply.



**Figure 2.** A prototype mini tandem accelerator-based neutron/gamma generator. Photo captured by the authors.

By operating the mini tube near the threshold energy (1.88 MeV) of the  $p\text{-}^7\text{Li}$  reaction, the neutrons produced have an epithermal energy distribution which is useful for BNCT application.<sup>6</sup> By biasing the carbon stripping foil at +950 kV, the  $\text{H}^+$  ions will interact with the lithium target at an energy of 1.9 MeV. The epithermal neutron yield is  $5 \times 10^8$  n/s for an  $\text{H}^+$  ion beam current of 2.5 mA and at 1% duty factor pulsed operation.<sup>6</sup> To enhance the epithermal neutron output, a cluster of these mini neutron tubes can be employed. This multiple neutron tube arrangement will greatly reduce the BNCT treatment time.<sup>7</sup>

Similarly, one can employ the  $p\text{-}^{19}\text{F}$  reaction to generate 6 MeV gamma photons for cancer radiotherapy purposes.<sup>7</sup> With the tandem accelerator arrangement, the mini gamma tube can achieve 2 MeV interaction energy using a 1 MV high-voltage pulser. A single mini gamma tube can produce about  $1.6 \times 10^9$   $\gamma$ /s for 1% duty factor pulsed operation.<sup>8</sup> At 2 cm, the gamma flux is  $3.2 \times 10^7$   $\gamma/\text{cm}^2/\text{s}$ . Operating with a cluster of seven mini tubes, the combined gamma flux becomes  $2.2 \times 10^8$   $\gamma/\text{cm}^2/\text{s}$  for 1% duty factor. This gamma flux can be improved by one order of magnitude if the duty factor is increased to 10% or by increasing the high voltage from 1 to 1.5 MV.<sup>8</sup> The gamma flux (at 2 cm) will become  $2.2 \times 10^9$   $\gamma/\text{cm}^2/\text{s}$  which is about the same as the Gamma Knife.<sup>7</sup>

### 3.2. Application of the tandem accelerator-based mini neutron/gamma/proton tube in brachytherapy

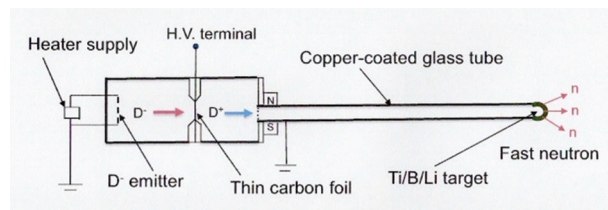
In brachytherapy, the radiation source is either placed directly inside the tumor (interstitial brachytherapy) or in the vicinity of the tumor (intracavity brachytherapy). Compared with an external beam irradiation treatment, brachytherapy has the advantage of delivering a high radiation dose to a localized cancer tissues and minimizing the damage to healthy tissues. Conventional gamma/neutron brachytherapy utilizes small pellets of radioisotopes (such as  $^{125}\text{I}$ ,  $^{192}\text{Ir}$ ,  $^{60}\text{Co}$ ,  $^{137}\text{Cs}$ , or  $^{252}\text{Cf}$ ) as radiation sources. For a low-dose-rate source with short half-life radioisotopes, the pellets can be permanently implanted into the patient. For a high-dose-rate source with a longer half-life, the pellets are loaded into the tumor with a catheter. They are removed from the patient after the irradiation process is completed.

Accelerator-based neutron generators have been considered for neutron brachytherapy application.<sup>5</sup> These positive ion-based generators employ a radiofrequency plasma source to provide the deuterium ions needed for producing either d-d or d-t neutrons. The radiofrequency plasma source and its associated power supply and matching circuit can occupy a large space, making the system difficult to manipulate

during the irradiation process. On the other hand, the mini tandem accelerator-based neutron/gamma tube is small and only requires a single heater power supply for H/D generation. More importantly, the chamber containing the high-voltage carbon stripper foil is located outside the patient's body, while the target electrode, where neutrons/gammas are formed, is at ground potential. With this mini tandem accelerator arrangement, one can safely perform various types of brachytherapy for cancer treatment.

#### 3.2.1. Mini tandem accelerator tube for fast neutron brachytherapy

Figure 3 shows a schematic diagram of a mini tandem accelerator neutron tube designed for fast neutron brachytherapy application. The dimension of the mini tandem accelerator tube is 3 cm  $\times$  6 cm (diameter  $\times$  length). Unlike the tandem accelerator tube shown in Figure 1, this mini neutron generator has a long narrow copper tube for insertion into the tumor of the patient. This copper tube is about 4 mm in diameter and 12 cm in length. For fast neutron brachytherapy, either d-d, d- $^{10}\text{B}$  or d- $^7\text{Li}$  neutrons can be employed. As the d- $^7\text{Li}$  reaction produces the highest neutron energy and output dose, a small lithium target is installed at the end of the narrow tube. A copper mesh (with transparency >90%) is mounted at the entrance of the narrow copper tube to define an equipotential surface. The mesh, copper tube, and Li target are all biased at ground potential. On leaving the carbon foil, the  $\text{D}^+$  ions accelerate to the copper mesh and reach the Li target after traveling down the copper tube. Fast 10 and 13 MeV neutrons are generated by the d- $^7\text{Li}$  reaction. With a 2 MV, 0.4 mA  $\text{D}^+$  beam, the total d- $^7\text{Li}$  neutron yield is about  $6 \times 10^{11}$  n/s. For 1% duty factor operation, the average neutron yield is  $6 \times 10^9$  n/s. For comparison, one milligram of  $^{252}\text{Cf}$  emits  $2.3 \times 10^9$  n/s. In the United States, about 100  $\mu\text{g}$  of  $^{252}\text{Cf}$  has been employed in fast neutron brachytherapy.<sup>5</sup> A pair of permanent magnets is installed at the copper tube entrance. The magnetic field ( $\sim 150$  Gauss) generated by these magnets will prevent secondary emission electrons from leaving the tube.



**Figure 3.** A mini tandem accelerator-based neutron tube for fast neutron brachytherapy. Schematic created by the authors. Abbreviation: H.V.: High-voltage.

### 3.2.2. Mini tandem accelerator tube for BNCT brachytherapy

BNCT is based on the high probability of a stable isotope  $^{10}\text{B}$  capturing a thermal neutron, thereby releasing two high-energy ions ( $^4\text{He}^{2+}$  and  $^7\text{Li}^+$ ). Due to the high linear energy transfer and relative biological effectiveness of these ions, only cells near the reaction  $^{10}\text{B}(n,\alpha)^7\text{Li}$  are damaged, leaving adjacent cells unaffected. The enhanced uptake of the boron-labeled agent in tumor cells versus normal cells results in selective killing of tumor cells. To perform BNCT brachytherapy, one can employ the  $p\text{-}^7\text{Li}$  reaction, which can provide neutrons with epithermal energy (0.5 eV to 20 keV) by operating near the threshold energy of 1.88 MeV.<sup>6</sup> These epithermal neutrons will convert into thermal neutrons as they pass through the body tissues. The high capturing cross-section of the thermal neutrons by the  $^{10}\text{B}$  atoms results in the production of the energetic  $^4\text{He}^{2+}$  and  $^7\text{Li}^+$  ions that will kill the tumor cells effectively. It is estimated that the  $\text{H}^+$  beam current reaching the Li target is about 0.4 mA. The time average epithermal neutron produced will be about  $0.6 \times 10^8$  n/s for 1% duty factor operation.

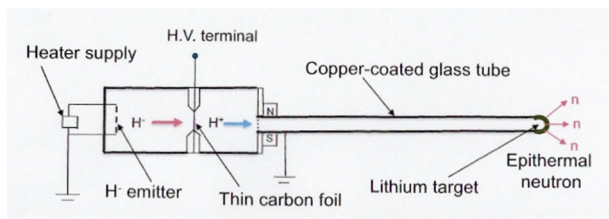
The use of the coaxial-type mini neutron generator for BNCT brachytherapy has been previously reported.<sup>9</sup> If a small-diameter neutron tube is needed for BNCT brachytherapy, the mini tandem accelerator tube can provide the required configuration for epithermal neutron generation. Figure 4 shows the schematic diagram of a mini tandem accelerator-based epithermal neutron tube for BNCT brachytherapy. Unlike the fast neutron tube,  $\text{H}^+$  ions are initially produced at the titanium foil. By applying +950 kV high-voltage pulses at the carbon stripping foil, the  $\text{H}^+$  ions formed will accelerate into the lithium target located at the end of the copper tube with an energy of 1.9 MeV. By inserting the tube *inside* the tumor, epithermal neutrons produced through the  $p\text{-}^7\text{Li}$  reaction at the end of the narrow tube will be converted into thermal neutrons as they move outward. This tandem accelerator brachytherapy tube provides some advantages over the external epithermal neutron beam arrangement. The damage of the healthy tissues along the neutron beam

path is minimized while BNCT treatment is more localized at the tumor site.

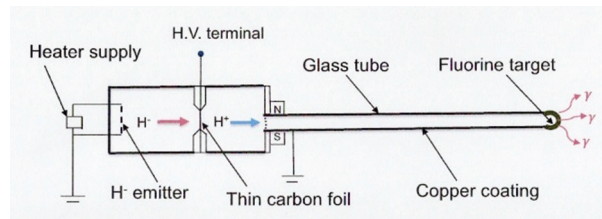
### 3.2.3. Mini tandem accelerator tube for gamma brachytherapy

Gamma photon brachytherapy is commonly performed in clinical facilities by using radioactive sources such as  $^{137}\text{Cs}$  and  $^{192}\text{Ir}$ . The energy of the emitted gamma photons ranges from 400 to 600 keV. Low-energy gamma sources such as  $^{103}\text{Pd}$  and  $^{125}\text{I}$  are used in permanent implant of prostate tumors. These low-energy gamma sources require fewer shielding materials and spare more healthy tissue. They also have higher relative biological effectiveness. The mean photon energies of  $^{102}\text{Pd}$ ,  $^{125}\text{I}$ , and  $^{241}\text{Am}$  are 21 keV, 28 keV, and 60 keV, respectively. Their relative biological effectiveness values are 2.3, 2.1, and 2.1, respectively. Small sources are normally delivered into the tumor by a remote after-loading device to avoid unnecessary occupational dose to the clinical personnel.<sup>5</sup>

The mini tandem accelerator gamma brachytherapy tube can produce both low- and high-energy gamma photons through nuclear reactions. Most of these reactions produce both gammas and neutrons simultaneously. As an example, the  $^6\text{Li}(d,n\gamma)^7\text{Be}$  produces 480 keV gammas as well as fast neutrons. Some reactions, however, only produce gamma photons. The  $p\text{-}^{19}\text{F}$  reaction, for example, produces mono-energetic 6 MeV gamma photons. At 2 MeV interaction energy, the gamma yield is  $6 \times 10^{10}$   $\gamma/\text{mA}\cdot\text{s}$ .<sup>8</sup> For 1% duty factor operation, the average gamma yield becomes  $6 \times 10^8$   $\gamma/\text{mA}\cdot\text{s}$ . Figure 5 shows the schematic diagram of a mini tandem accelerator gamma brachytherapy tube. The  $\text{H}^+$  ions are accelerated to 2 MeV down the copper tube, and they interact with the fluorine target to produce the 6 MeV gammas. Thin layers of  $\text{CaF}_2$  or  $\text{MgF}_2$  can serve as the target material. The gamma dose delivered to the tumor can be controlled by adjusting the ion beam on-time. To produce lower-energy gammas, one can operate the tandem accelerator tube with the  $p\text{-}^7\text{Li}$  reaction at proton beam energy just below 1.88 MeV. The reaction generates only 480 keV gammas. For 1% duty factor operation, the average gamma yield is about  $2 \times 10^9$   $\gamma/\text{mA}\cdot\text{s}$ .<sup>10</sup>



**Figure 4.** A mini tandem accelerator-based epithermal neutron tube for BNCT brachytherapy. Schematic created by the authors. Abbreviations: BNCT: Boron neutron capture therapy; H.V.: High-voltage.



**Figure 5.** A mini tandem accelerator-based gamma-ray tube for gamma brachytherapy. Schematic created by the authors. Abbreviation: H.V.: High-voltage.

### 3.2.4. Mini tandem accelerator tube for proton brachytherapy

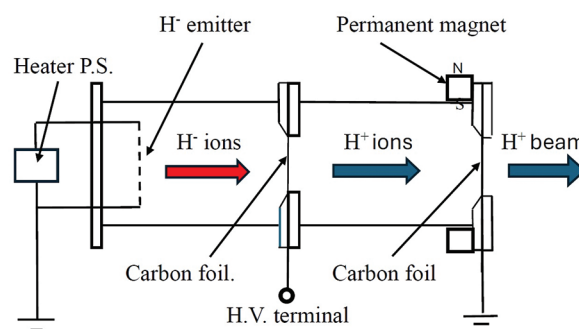
Protons can be used to treat cancer patients. Unlike other radiation particles, protons deposit most of their energy toward the end of their path in a medium, resulting in a peak in the dose distribution known as the Bragg Peak. This phenomenon maximizes damage to cancerous cells while sparing healthy tissue. Proton therapy is normally performed in complex and large accelerator systems such as cyclotrons and synchrotrons. Compared with other radiation particles (such as photons and neutrons), the range of protons in a human body is very short. Table 2 shows the range of a proton in water (where the Bragg Peak occurs) for energies between 10 and 200 MeV.<sup>11</sup> To reach the tumor located at the center of a human body, protons with energies >200 MeV are required. In addition, a large bending magnet is needed to direct the proton beam to the patient's tumor from multiple angles. The magnet is mounted on a large structure, called the gantry. The gantry rotates 360° around the patient during the treatment process. The complete proton therapy system is expensive to build. It occupies a large space and requires a large crew to operate.

The tandem accelerator-based proton (or deuteron) tube is very compact and much easier to operate. Figure 6 is a schematic of a tandem accelerator proton tube. By replacing the target electrode with a thin carbon foil, the accelerated H<sup>+</sup> ions emerge from the foil as a proton beam. However, the tandem accelerator tube can provide proton beams of much lower energy compared to those produced by the big accelerator systems; therefore, their penetration into the patient's body is very shallow. As a result, they are not useful for external proton beam therapy. To reach the tumor site, the proton source must be placed inside or near the tumor to perform proton brachytherapy. For a 2 MeV proton beam, the range in water is only several hundred micrometers. However, the range increases to 4.3 mm for a 20 MeV proton. This range can be useful for the treatment of small-size tumors. To perform proton therapy on a cancer tumor, the location of the Bragg Peak can be adjusted by varying the proton beam energy or simply by moving the brachytherapy tube. This operational procedure will ensure that the entire tumor is treated by the Bragg Peak.

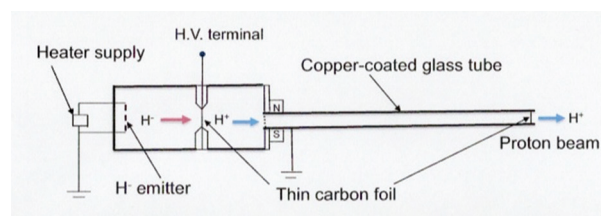
Figure 7 shows the design of a 20 MeV tandem accelerator tube for proton brachytherapy. There are two thin carbon foils in this proton brachytherapy tool. The first carbon foil is connected to a 10 MV pulser. The second foil and the copper tube are biased at ground potential. A pair of permanent magnets at the tube entrance will prevent secondary emission electrons from streaming back to the high voltage foil. For a 4-mm-diameter copper

**Table 2. Range of a proton in water for energies between 10 and 200 MeV calculated from the NIST PSTAR database**

| Proton energy (MeV) | Range in water (mm) |
|---------------------|---------------------|
| 10                  | 1.23                |
| 20                  | 4.26                |
| 30                  | 8.85                |
| 40                  | 14.89               |
| 50                  | 22.27               |
| 100                 | 77.18               |
| 150                 | 157.70              |
| 200                 | 259.60              |



**Figure 6.** A tandem accelerator-based proton tube for high-energy proton beam production. Schematic created by the authors. Abbreviations: H.V.: High-voltage; P.S.: Power supply.



**Figure 7.** A mini tandem accelerator-based proton tube for proton brachytherapy. Schematic created by the authors. Abbreviation: H.V.: High-voltage.

tube, the average transmitted H<sup>+</sup> current is about 4 μA for 1% duty factor operation. The proton dose exiting the tube is about 2.5 × 10<sup>13</sup> proton per second. If a higher voltage pulser (>10 MV) can be developed, this brachytherapy system will offer an alternative approach for the treatment of cancer through proton therapy.

## 4. Conclusion

Mini tandem accelerator tubes can be operated with D<sup>+</sup> or H<sup>+</sup> ion beams to produce a high flux of neutrons, gammas, or protons for cancer therapy applications. The mini accelerator tube employs a high-frequency AC high-

voltage power supply and a thin carbon foil for stripping of H/D<sup>+</sup> to form H<sup>+</sup>/D<sup>+</sup> ions. When operated with a narrow insertion tube, the neutrons or gamma-photons produced can be used for brachytherapy treatment inside or near the tumor. If the biasing voltage of the stripper foil is higher than 10 MV, proton beams with a range greater than 4.2 mm can be used for proton brachytherapy treatment of cancer. Compare with costly, large-scale cyclotron and synchrotron systems, this proton therapy tool is simpler and readily deployable in hospitals and clinical facilities.

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## Conflict of interest

The authors declare that they have no competing interests.

## Author contributions

*Conceptualization:* All authors

*Investigation:* All authors

*Methodology:* All authors

*Writing—original draft:* Ka-Ngo Leung

*Writing—review & editing:* James K. Leung

## Ethics approval and consent to participate

Not applicable.

## Consent for publication

Not applicable.

## Availability of data

Data are available from the corresponding author on reasonable request.

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