Mobetron® 1000

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EXECUTIVE SUMMARY

Introduction

Intraoperative radiation therapy (IORT) is the delivery of a single large radiation dose to the tumor bed during surgical resection with the final goal of enhancing locoregional tumor control. During IORT, the normal or uninvolved tissues are not exposed to radiation because they are removed or shielded from the treatment field. IORT has been customarily performed either in a shielded operating suite located within or adjacent to the operating room (OR) or in a shielded treatment room located within the Department of Radiation Oncology using stationary linear accelerators. There is a need to transport patient from operating room to the radiation oncology department for treatment. The logistics of such procedure and possible complications from anaesthesia and wound infection hindered widespread implementation of IORT programs. With advancement of technology, mobile linear accelerators that can be used in existing ORs with reduced shielding requirements, cost and logistics have been developed. This technology review was requested by Director of Medical Development Division.

Objective/Aim

To determine the safety, effectiveness and cost effectiveness of Mobetron® 1000 for intraoperative radiotherapy.

Results and conclusion

There was limited evidence on the effectiveness and safety of Mobetron® 1000 for intraoperative radiotherapy. As for cost-effectiveness there is no retrievable evidence.

Methods

Scientific electronic databases which include Pubmed, Proquest, EBSCO Host, Medline, CINAHL, Science Direct, Cochrane database of systematic reviews, HTA databases, Horizon scanning databases and FDA website were searched.

Mobetron® 1000

1. INTRODUCTION

The earliest concept of intraoperative radiation therapy (IORT) as a cancer treatment modality was introduced in 1909, when Carl Beck attempted to treat patients with gastric and colon cancer. However, it was not until 1984 in Japan, that IORT treatment techniques using megavoltage radiation produced by a linear accelerator (linac) became successful. Since then, there has been substantial progress in the application of intraoperative radiation therapy (IORT) as a treatment modality for abdominal, pelvic, head and neck, and thoracic cancers, and more recently breast neoplasms.[1]

Intraoperative radiation therapy (IORT) is the delivery of a single large radiation dose to the tumor bed during surgical resection with the final goal of enhancing locoregional tumor control. During IORT, the normal or uninvolved tissues are not exposed to radiation because they are removed or shielded from the treatment field. IORT can be delivered by electron beams produced by linear accelerators (also called IOERT), or high-dose rate brachytherapy (HDR-IORT). IORT is performed with applicators and cones that attach to the treatment head of high-energy medical linear accelerators that are designed to direct radiation to defined surface structures. [1, 2]

Intraoperative radiation therapy has been customarily performed either in a shielded operating suite located within or adjacent to the operating room (OR) or in a shielded treatment room located within the Department of Radiation Oncology. In both cases, this cancer treatment modality uses stationary linear accelerators. Therefore there was a need to transport patient from operating room to the radiation oncology department for treatment. The logistics of such procedure and possible complications from anaesthesia and wound infection hindered widespread implementation of IORT programs. Another major limiting factor is the cost associated with outfitting a dedicated room with proper shielding, purchase of a linear accelerator dedicated for use in the operating room, and construction of a separate IORT suite adjacent to the operating room. However, new technologies have provided a more cost effective approach.[1, 3]

With the development of new technology, mobile linear accelerators (linacs) have recently become available for IORT. These mobile accelerator units, which can be transported any day of use to almost any location within a hospital setting, are assembled in a nondedicated environment and used to deliver IORT. Thus, mobile linacs that can be used in existing ORs with reduced shielding requirements makes the cost and logistics of setting up an IORT program much easier. Currently available principle mobile linacs are Novac7, Mobetron and Liac.[1]

This technology review was requested by Director of Medical Development Division following request from a company to supply this device to Ministry of Health facilities.

2. OBJECTIVE/AIM

The objective of this review was to determine the safety, effectiveness and cost effectiveness of Mobetron® 1000 for intraoperative radiotherapy.

3. TECHNICAL FEATURES

Fig 1: The Mobetron unit

Fig 2: Applicators ranging from 3 to 10 cm

Mobetron® is a registered trademark of IntraOp Medical, Inc. It is a mobile electron beam intraoperative treatment system designed for electron beam radiotherapy treatments in the operating room. The Mobetron system consists of a lightweight linear accelerator based on X-band technology (3 cm wavelength, 10 GHz frequency) compared to S-band technology (10 cm wavelength, 3 GHz frequency) in the conventional linear accelerator which is heavier. The use of X-band technology eliminates the use of bending magnets which is the source of stray radiation. Mobetron is mounted on a motor-driven C-arm gantry. The gantry may be rotated ± 45º downward in the transverse plane, tilted ± 30º in the radial plane and translated in a horizontal plane ± 5 cm. The gantry tilt and horizontal movement is a unique feature not found in conventional accelerators used for intraoperative radiotherapy. The Mobetron uses a soft-docking system in which the gantry is optically guided to a position 4 cm above the applicator. A beamstopper is mounted opposite to the accelerator to intercept radiation produced in the forward direction. The maximum height and length dimensions are 250 cm and 290 cm with a weight of 1140 kg. For transportation the gantry can be stored in the C-arm giving a height of 190 cm. This permits transportation in elevators. [3,4,5]

The Mobetron system is composed of three separate units: the control console, the modulator, and treatment unit. The control console operates the accelerator during radiation treatment delivery. It is placed outside the operation room so that the radiation treatment delivery is controlled remotely. The modulator contains the electronic system of the accelerator and energizes the accelerator to produce electron beams. The Mobetron system produces four levels of energy, 4, 6, 9 and 12 Million Electron Volts (MeV) with therapeutic ranges up to 4 cm. The system is designed to deliver a very large, uniform dose of 10 Gy to 25 Gy in a single fraction at a dose rate of 10 Gy/min. Treatments are delivered using either flat or bevelled circular applicators with diameters extending from 3 to 10 cm. Flat applicators are used for sites where treatment areas are predominantly flat, and bevelled applicators are used to treat sites which present at an angle. The length of applicators is 30 cm and the source-to-skin distance (SSD) is 50 cm. The design of the accelerator (patented energy-control system without bending magnets) and treatment applicators, in combination with the lead beamstopper below the surgical table, allow the Mobetron to operate without additional shielding in the operating room. This device is classified as class II medical device and has obtained FDA approval. Currently the Mobetron mobile IORT system is used in several countries as shown in Table 1.[3,4,5]

Table 1: Sites using the Mobetron mobile accelerator system

Country	Institution	Year of Installation
Unites States	University of California San Francisco	1997
	University Hospital of Cleveland	1999
	University of Lousville	2000
	University of North Carolina	2001
	Mayo Clinic	2002
	Methodist Hospital of Indianapolis	2002
	Ohio State University Hospital	2004
Netherlands	Catharina-ziekenhuis	2003
Poland	University Hospital, Krakow	2003
Spain	Hospital San Jaime, Torrevieja	2004
Italy	Ospedale Maggiore della Carita, Novara	2005
Japan	Nagoya University Hospital	2006
	Gunma Prefectural Cancer Center	2007
Germany	CDT Strahleninstitut Koln, Cologne	2007

4. METHODOLOGY

4.1. Searching

Electronic databases which include Pubmed, Proquest, EBSCO Host, Medline, CINAHL, Science Direct, Cochrane Database of Systematic Reviews, HTA Databases, Horizon Scanning databases and FDA website were searched. There was no limitation in the search. The following keywords were used either singly or in combinations: Mobetron, mobile linear accelerator, intraoperative radiotherapy, cost*, safe*, effectiveness.

4.2. Selection

All published articles related to safety, effectiveness, and cost effectiveness of mobile linear accelerators for intraoperative radiotherapy were included. The articles retrieved include cross sectional and experimental studies. All relevant literature was critically appraised and graded according to US/Canadian Preventive Services Task Force.

5. RESULTS AND DISCUSSION

5.1. SAFETY

Personnel protection and requirements of shielding is a concern with the use of devices for intraoperative radiotherapy. The AAPM recently published recommendations for the implementation of an IORT program using mobile linear accelerators in a non-dedicated environment. In particular, it recommended that a radiation survey around the ORs used for IORT be mandatory, to ensure that the maximum exposure limits in the adjacent areas are not exceeded.[2 Level III] The major source of radiation leakage in conventional accelerators is bending magnet. The Mobetron uses X band technology which eliminates the need for bending magnet. This causes a reduction in photon leakage. However, the Mobetron has two points of potential leakage: the area where the two collinear accelerators meet and the scattering foil.[6 Level II-3]

Daves and Mills performed a detailed analysis of the shielding assessment on a Mobetron unit. Their exposure rate measurements data indicated that the Mobetron may be operated in an area with no shielding under a nominal patient load expectation. Assuming standard building materials, their results demonstrated that a workload of three to four patients per week in a given OR, including warmup, could be easily accommodated.[6 Level II-3] This is supported with another study by Mills *et al.* who reported that it is possible to treat up to four patients per week in an unshielded OR using the Mobetron system. If mobile IORT units are to be used without workload limitations, then they should only be used in shielded ORs.[5 Level II-3 ,6 Level II-3] In Japan, Nakagawa *et al.* did a leakage measurement for a dose of 240 Gy, which corresponds to the maximum recommended weekly dose in IORT using Mobetron. The leakage dose level in the controlled area was less than 300 µSv/week (0.3 mSv/week), which is within recommended limit. However, based on the

current workload the leakage dose in the uncontrolled area was beyond limit of 1 mSv/year. Thus additional shielding was required.[7 Level II-3] In the United States, the allowable exposure level for uncontrolled areas is 1 mSv/year and for controlled area is 1 mSv/week (50 mSv/year).[2 Level III]

Loi *et al*. compared the neutron production at 12 MeV from Mobetron with conventional accelerator. The primary process for neutron production by an electron beam is the absorption of the bremsstrahlung photons (a type of electromagnetic radiation) produced by the electrons. Loi *et al*. found that neutron dose equivalent rates generated from Mobetron are at least one order of magnitude lower than conventional linear accelerator operated at the same energy in electron mode. Therefore their measurements showed that Mobetron can be used at 12 MeV in an unshielded OR for a weekly workload up to 250 Gy if the bremsstrahlung x-rays are appropriately shielded to negligible levels.[8 Level II-3]

5.2. EFFECTIVENESS

A retrospective review of colorectal cancer patients treated since 1999 with IORT using Mobetron device was conducted by Williams *et al*. The study included 40 patients with either a primary or secondary malignancy with colonic or rectal involvement. All patients underwent surgical resection. There was no significant difference regarding crude survival in patients with microscopically positive margins, those with fibrosis or mucin at margin, or those with negative margins (p=0.41). Mean survival was 35 ± 26 months. Local recurrence occurred only in one patient. The most common complications encountered was bladder dysfunction and urinary tract infection.[9 Level II-3] The outcomes of this study using mobile accelerator are comparable to other studies on IORT using conventional linacs.[10 Level II-2, 11, 12]

Hashiguchi *et al*. analyzed the applicability of mobile linear accelerator Mobetron based on its specification by simulating the intraoperative radiation therapy delivered to patients with a conventional intraoperative radiation therapy unit. A total of 49 patients with colorectal cancer underwent surgical resection and IORT. The IORT patients were divided into two groups; Group L received IORT of 12 MeV or less (dose of 22 Gy) and Group H received IORT exceeding 12 MeV (dose of 25 Gy). Thirty percent of patients in this study were delivered with an electron energy level exceeding 12 MeV. An energy level of 12 MeV gives about 4 cm clinical treatment depth. Therefore, 12 MeV energy level is not adequate in patients with gross residual tumour. In conclusion, the mobile accelerator Mobetron can cover 72 percent of the irradiation sites covered by conventional unit. The electron energy level of Mobetron is sufficient and suitable for microscopic tumours.[13 Level II-3]

Stability is a concern due to the differences in mobile accelerators systems that allow their transportability. In order to test the short and long term stability of Mobetron unit, Beddar S conducted a study in 2005 concerning reproducibility and energy stability for 20 pretreatment QA trials over a 5 month period. For daily QA tests, the output did not vary more than ±2% for all energies. The energy variations resulted in a shift of less than

1 mm on the depth-dose curve. The dose output stability of Mobetron when it was powered and stayed idle overnight in the operating room, as well as throughout an 8 hour period of inactivity during the day found to vary by less than 1% overnight and 1.1% or less during the day. Thus, the short and long term reproducibility and stability of Mobetron is well within specifications and comparable to conventional linear accelerators.[14 Level II-3]

5.3. COST / COST- EFFECTIVENESS

There was no retrievable evidence on the cost effectiveness of using Mobetron® 1000 for intraoperative radiotherapy.

In the United States, the cost of Mobetron unit is [redacted]. Mobetron requires three-phase electrical power which costs about [redacted] for an operating room. However, there is no construction cost involved for Mobetron. A conventional IORT unit costs about [redacted] It requires construction of a shielded operating room with costs approximating [redacted] to [redacted]. Therefore overall cost of installation for conventional unit is more compared to Mobetron.[13 Level II-3]

5.4 ORGANIZATIONAL ISSUES

Intraoperative radiotherapy is recommended for locally advanced tumours. Therefore it is not widely applicable in Malaysian context as majority of patients present with advanced cancer. Furthermore, our oncologists have no experience in delivering IORT.

6. CONCLUSION

There is limited evidence on the effectiveness and safety of Mobetron® 1000 for intraoperative radiotherapy. However, there is no evidence on the cost effectiveness of using Mobetron® 1000 for intraoperative radiotherapy.

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8. APPENDIX

DESIGNATION OF LEVELS OF EVIDENCE

I Evidence obtained from at least one properly designed randomized controlled trial.

II-I Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)