Available online at http://www.biij.org/2007/3/e57
doi: 10.2349/biij.3.3.e57

Biomedical Imaging and Intervention Journal
COMMENTARY

Pioneering innovative radiation oncology technology in clinics

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Received 4 February 2008; received in revised form 8 April 2008; accepted 15 April 2008

ABSTRACT

Pioneering and implementing new technology successfully in a radiation oncology clinic requires hard work, team effort and management support. Over the last 15 years, we have pioneered the clinical implementation of intensity-modulated radiation therapy (IMRT) as well as combined radio-gene-therapy in the treatment of cancer. The entire department including physicists, dosimetrists, therapists, nurses, managers, data managers, radiation oncologists and residents in training, other medical specialists e.g. neurosurgeons, urologists, pathologists, radiologists, molecular biologists and many others have joined forces and contributed to the success. IMRT has transitioned from an initial experimental approach to a standard of care approach now in various disease sites. We are entering a new era of image-guided radiation therapy (IGRT) and molecular-targeted therapy and we continue to strive to implement these new technologies in the clinics. Frameless stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) have now become a clinical reality. Again, all these require a tremendous amount of efficient management and cooperation among all departmental staff. Five fundamental principles which can help the successful pioneering and implementation of innovative radiation oncology approaches will be discussed. These include identifying a project champion(s), pursuing a multi-disciplinary approach, showing clinical efficacy and return on investment (ROI), ability to articulate the project and celebrating the successful implementation.

Keywords: Pioneering, innovative, technology, radiation oncology, intensity modulated radiation therapy (IMRT)

INTRODUCTION

Tremendous advances in both physics and biology have taken place in radiation oncology over the last 20-30 years. For external beam radiotherapy, we have progressed from ortho-voltage machines to mega-voltage linear accelerators and now image-guided linear accelerators. For radiation dosimetry planning and

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delivery, we have also progressed from a simple hand calculation method of one field or parallel opposed fields to multi-field three-dimensional conformal radiotherapy (3D-CRT) to intensity-modulated radiation therapy (IMRT) and more recently image-guided radiation therapy (IGRT) and stereotactic body radiation therapy (SBRT) [1-4]. Integrating advances in molecular biology and targeted therapy in the field of radiation oncology has also seen improvement in treatment outcome [5]. The advances in radiation oncology approaches encompassing physics, biology and clinical aspects have shown significant positive impact in cancer care from improving local control to decreasing treatment-related side effects leading to better quality of life and ultimately prolonged survival.

INNOVATIVE RADIATION ONCOLOGY APPROACHES IN CLINICS

Over the last 15 years, we have pioneered the clinical implementation of various radiation oncology approaches at our own institution. Several of these together with the associated outcome in radiation oncology will be highlighted here.

Intensity-modulated radiation therapy (IMRT)

The first patient was treated with IMRT in our department in March 1994, marking the beginning of clinical implementation of this new technology [1, 6]. IMRT has since thrived in radiation oncology and proved to be superior to the conventional radiotherapy or 3D-CRT in a few body sites especially head and neck, and prostate cancers. Since then, thousands of patients with various tumors involving different parts of the body have been treated with IMRT. We have demonstrated the efficacy of IMRT by a) decreasing xerostomia with a parotid-sparing approach (Figure 1) in head and neck cancer patients [7, 8], b) decreasing rectal toxicity in prostate cancer patients utilizing a rectal balloon for prostate immobilisation (Figure 2a & 2b) [9-13], c) decreasing ototoxicity in children with medulloblastoma (Figure 3) [14, 15] and d) improvement in tumor control by allowing dose escalation [16]. At our institution, we have also pioneered a new fractionation scheme with IMRT known as SMART (simultaneous modulated accelerated radiation therapy) boost (Figure 1) [17]. This new fractionation schedule was initially designed to overcome the rapid repopulation of tumor cells in head and neck cancer. SMART boost of different total doses allows us to treat the gross tumor and subclinical disease sites with different fraction sizes. It also allows the convenience of once-daily treatment as compared to other altered fractionation schemes requiring treatment two or three times a day to overcome rapid repopulation in head and neck cancers. In addition, re-irradiation with IMRT has become a reality [18, 19].

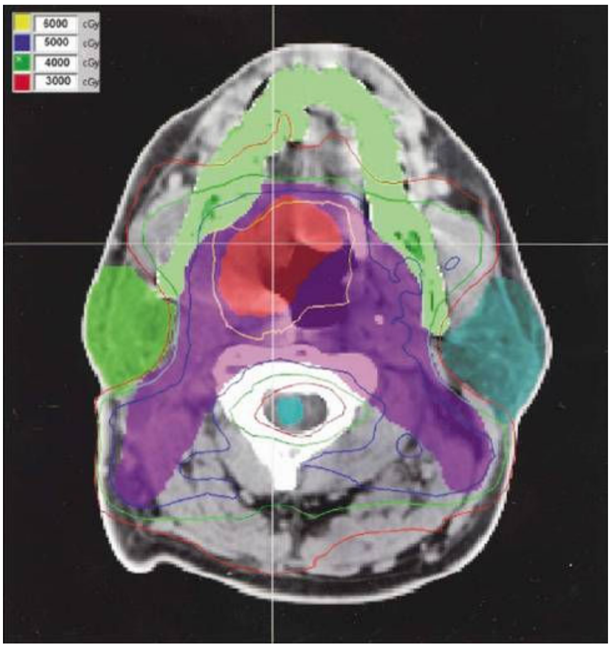

Figure 1 An axial image showing IMRT parotid sparing SMART boost approach in the treatment of head and neck cancer.

Combination radiation therapy and gene therapy / molecular targeted therapy

We have translated this approach from the laboratory to the clinics at our institution [20-23]. There are many potential benefits in combining radiotherapy with gene therapy as shown in (Table 1). Working closely with molecular biologists specializing in cell and gene therapy, we have demonstrated that combined radio-gene therapy increased tumor cell kill, suppressed distant metastases and prolonged survival in prostate cancer in animal models [24, 25]. This new form of spatial cooperation (two local therapy causing enhanced local and systemic effects) is likely due to the stimulation of immune system. This is also known as the active vaccine approach. Based on this principle, our phase I/II clinical trial in prostate cancer has shown that this is a promising approach and hopefully will be addressed in phase III trials. We have also observed the activation of immune cells e.g. CD4 and CD8 in patients receiving combined radio-gene therapy [26, 27].

Stereotactic radiosurgery (SRS) and fractionated stereotactic radiotherapy (SRT)

SRS and SRT program using BrainLab Novalis stereotactic system was started in our department in November 2003. This program required tremendous joint efforts from neurosurgeons and neuroradiologists in addition to our departmental efforts. Initially, we treated mainly patients with primary or metastatic brain tumors

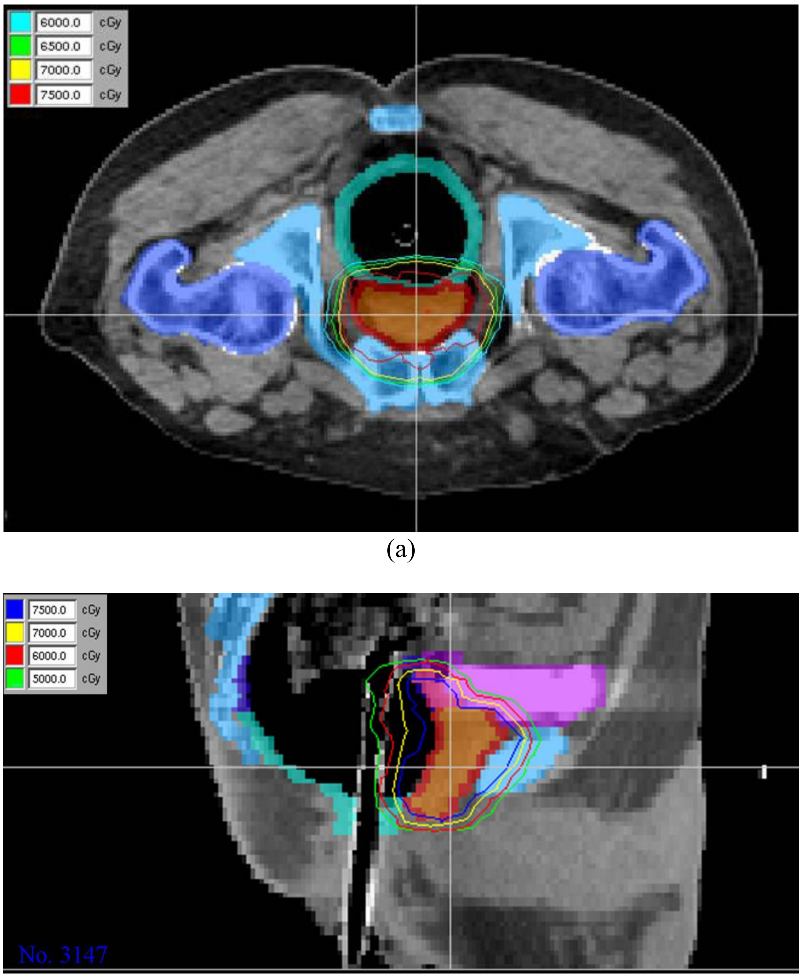

Figure 2 (a) Axial and (b) sagittal images showing IMRT utilizing rectal balloon for prostate immobilization in the treatment of prostate cancer – a rectal sparing approach

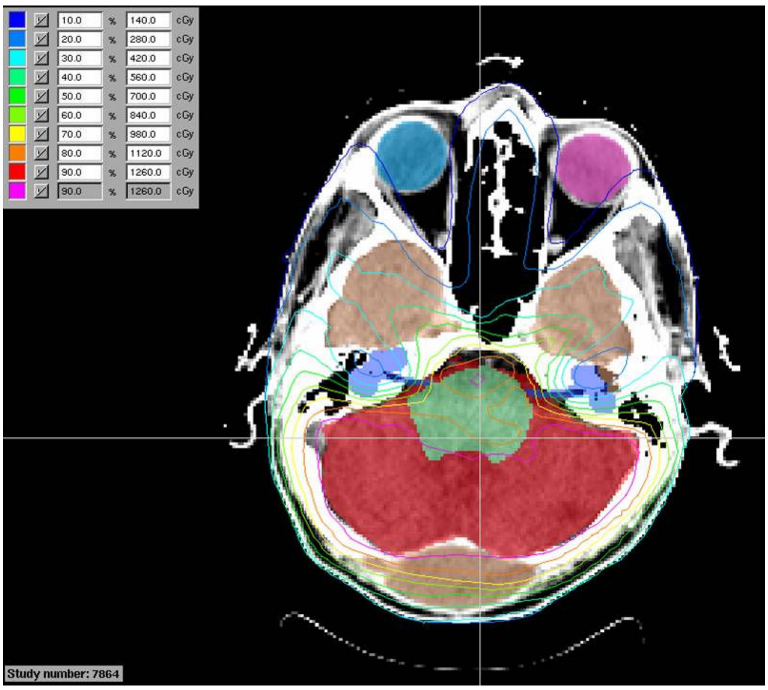

Figure 3 An axial image showing IMRT cranial nerve VIII sparing approach in the treatment of pediatric medulloblastoma.

Table 1 Potential benefits of combination radio-genetherapy (RT-GT).

Radiation improves transfection/transduction efficiency and transgene integration
Radiation may enhance the "bystander effect" of GT
Radiation and GT target at different phases of cell cycle
GT may increase DNA susceptibility to radiation damage
GT may interfere with repair of radiation induced DNA damage
Active vaccine approach

both benign and malignant, [28] but later proceeded to treat functional conditions such as trigeminal neuralgia.

Stereotactic body radiation therapy (SBRT)

Once we gained experience in SRS and SRT for cranial lesions, we embarked on stereotactic body radiation therapy (SBRT) for extracranial lesions using the BrainLab Novalis stereotactic system. At our institution, image-guidance with visicoils (Figure 4) and stereotaxis allow for the delivery of precise high-dose radiation in a few fractions, i.e. SBRT. SBRT, as defined by the American Society of Therapeutic Radiology and Oncology, and American College of Radiology practice guidelines is a treatment method that delivers a high dose of radiation to the target, utilizing either a single dose or a small number of fractions with a high degree of precision within the body [29]. Again, clinical implementation of this new technology requires the collaborative efforts of a multidisciplinary team in the department including radiation oncologists, medical physicists, radiation therapists, medical dosimetrists, nurses and administrative personnel. We have now shown that SBRT may play an important role in radio-resistant tumors such as renal cell carcinoma [4].

Image-guided radiation therapy (IGRT)

The advances in technology and physics in radiation oncology have led to clinical implementation of image-guided radiation therapy (IGRT). Because the surrounding normal tissues receiving high doses of radiation for IMRT is less compared to older technologies, the certainty of localisation of targets during treatment is very important. Image guidance before each treatment will improve the accuracy of radiotherapy delivery and avoid marginal misses/recurrences. We have implemented two different IGRT linear accelerators in our clinics, namely Helical Tomotherapy and BrainLab Novalis systems (Figures 4 & 5), which use megavoltage CT (MVCT) and kilovoltage X-Ray (KV X-Ray) for image-guidance. We have transitioned from IMRT using serial or sequential Tomotherapy (NOMOS system) to IGRT using Helical Tomotherapy (Figure 5). Helical Tomotherapy has now allowed us to treat tumors in almost all body sites encompassing larger areas, compared to initial treatment sites limited to prostate, brain, and head and neck. There is also no need for matching field approach with Helical Tomotherapy. This transition certainly requires teamwork but has significantly positive impact on patient care allowing more patients to receive and benefit from IMRT.

PET-CT fusion in radiation target delineation

PET-CT, combining anatomic and physiologic or functional imaging information, has made significant impact in oncologic imaging. We have also shown that the incorporation of PET-CT in radiotherapy target delineation has improved the accuracy, e.g. in identifying biologically active areas on PET-CT but negative on CT, decreased the target volume as PET-CT can help differentiate between active tumor and collapsed or consolidated lung [30-35]. Again, with the multidisciplinary involvement in the department, we have managed to implement PET-CT fusion in the target delineation in our clinics.

Computer visualisation techniques

Computer visualisation techniques (CVTs) are an emerging technology with the ability to maximize the currently untapped advantages of intensity-modulated radiotherapy (IMRT) (Figure 6) [36]. The visual speed and dynamic strategies inherent in CVTs improve IMRT by distilling vast amounts of anatomic, multimodal imaging, textual/meaning, and surgical/outcome data into a large, rigorous, standardised evidence base of storable target delineation plans. This ability to standardize strategies will allow the collection of meaningful evidence-based outcome data. Utilizing CVTs approach has fostered evidence-based target delineation and enhanced the accuracy in delineating GTV, CTV including draining lymphatics and normal tissues/avoidance structures in various anatomical sites. This system has important values in teaching nodal delineation to the residents and practicing radiation oncologists and it may also serve as a tool to standardize nodal delineation among participants across specialties

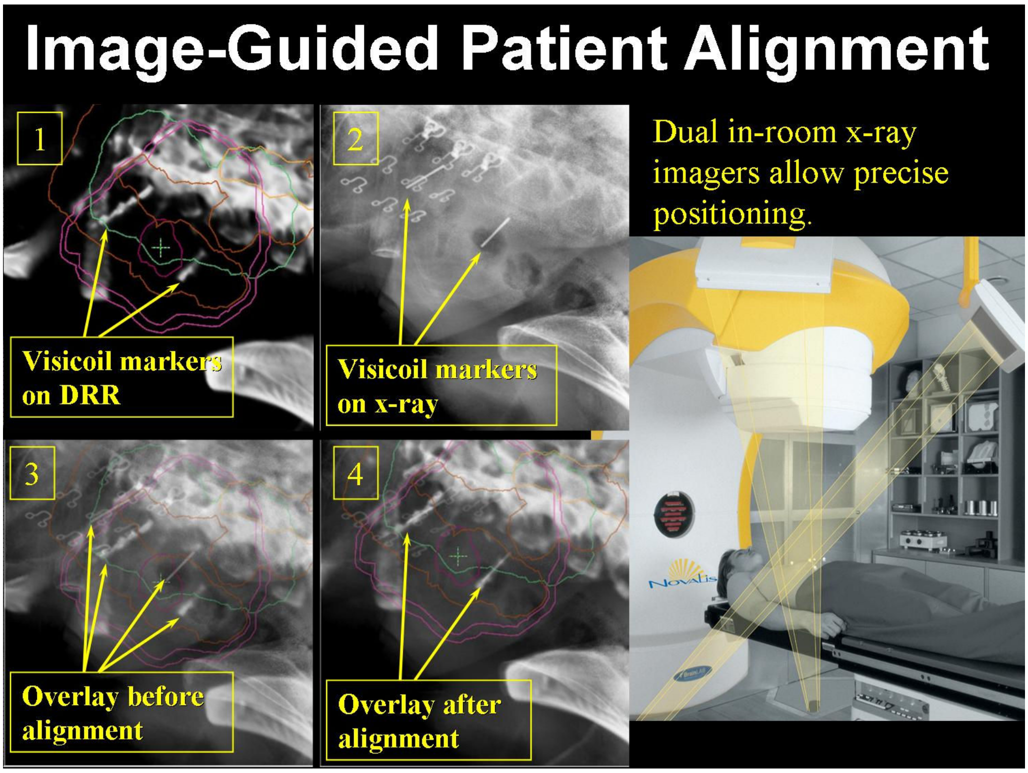

Figure 4 The Brainlab Novalis stereotactic linear accelerator includes two orthogonal diagnostic x-ray tubes and flat panel imagers to provide image-guided 3D patient alignment. Also note visicoil markers used for image-guidance in IGRT/SBRT.

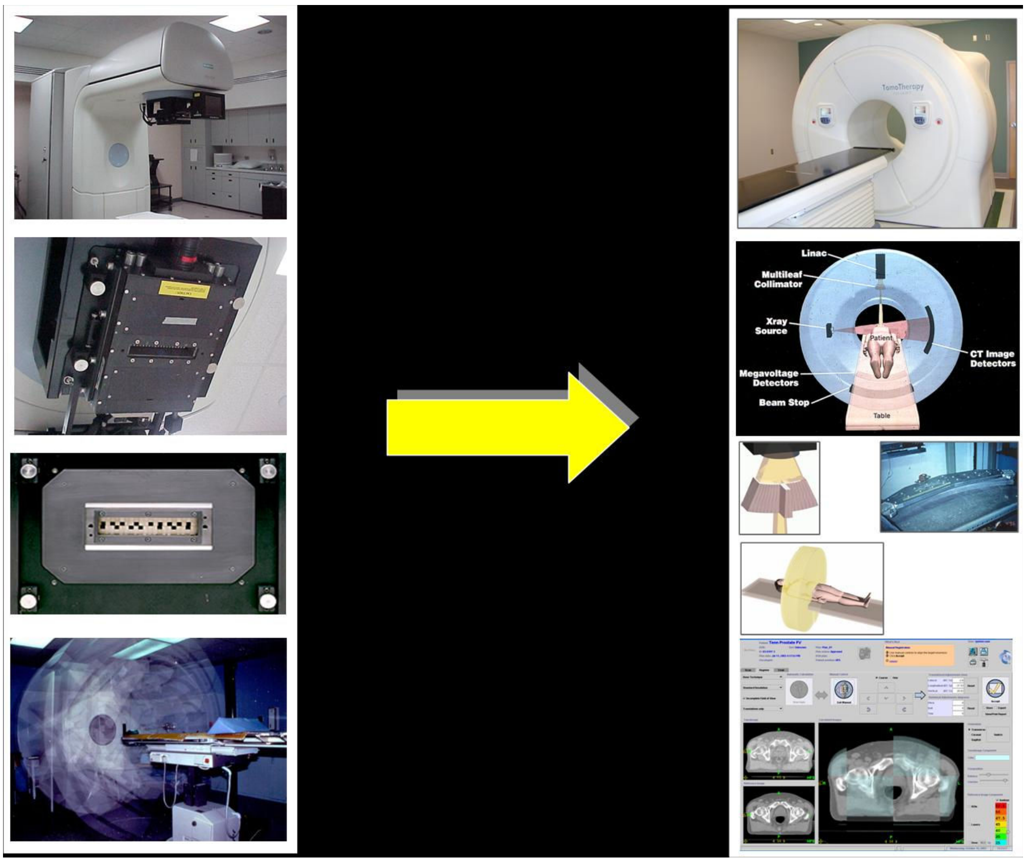

Figure 5 Transition from sequential tomotherapy (IMRT) to helical tomotherapy (IGRT).

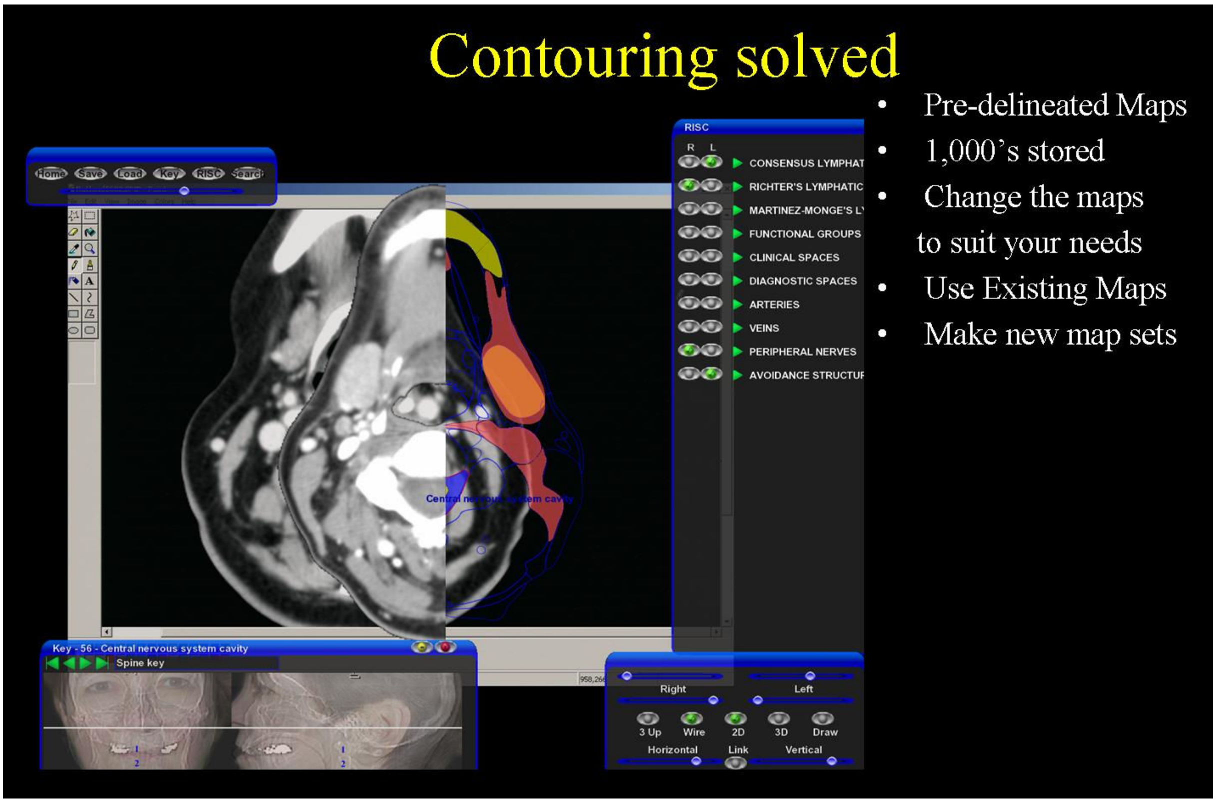

Figure 6 Computer visualisation techniques (CVTs) improve IMRT by distilling vast amounts of anatomic, multimodal imaging, textual/meaning, and surgical/outcome data into a large, rigorous, standardised evidence base of storable target delineation plans.

and training levels in multi-institutional trials addressing IMRT.

FIVE FUNDAMENTAL PRINCIPLES FOR SUCCESS

Implementing new technologies into a radiation oncology practice can be achieved successfully if a few fundamental principles are followed including: (1) identify a project champion; (2) approach it in a multi-disciplinary manner; (3) show clinical efficacy and return on investment (ROI) to all stakeholders; (4) be able to articulate the project concisely to those making the financial decisions; and (5) celebrate successful implementation. While these are relatively easy principles to grasp, not everyone adheres to them.

Identify a Project Champion(s)

Most, if not all, successful projects have a project champion or person who has the energy and passion to see an idea through from inception to implementation. These persons are usually willing to go the extra mile to ensure its success. They will give it their all and will do almost everything to answer all the questions decision makers ask and provide the entire team with up-to-date information. They are the driving force behind generating excitement about the project and spreading the word. A good example here is the success of clinical implementation of IMRT in our department. There was the commitment, determination, hard work and dedication of the medical director of the department in addition to working closely with the chief of medical physics and the administrative director. The project has an undertaking, with a clear beginning and end, usually aimed at creating some useful change or adding value. The skills needed to complete a project successfully are not required to manage a process and so project management has evolved as a discipline of its own. The successful project champion/manager has the ability to bring together all the right resources, and organize and manage the technology to a defined result. As with most successful projects, two-way communication is a requisite in order to perform on track. In other words, planning is conversation.

Approach it in a multi-disciplinary manner

Radiation oncology practices generally consist of radiation oncologists, medical physicists, radiation therapists, medical dosimetrists, nurses and administrative personnel. It is important for all disciplines who will be involved in the technology roll-out be involved from the front end of the process. This is highlighted again by our initial efforts in implementing IMRT clinically. We tried to achieve the best patient and target immobilisation by placing patients in immobilisation device, placing rectal balloon to minimize prostate motion and placing head screws on head and neck patients undergoing daily treatment. These were new endeavors requiring tremendous efforts from radiation oncologists, medical physicists, radiation therapists, medical dosimetrists, nurses and administrative personnel. Equally important is the involvement of the right people from across the organisation, like marketing, facilities, purchasing and your boss. The successful project champion/manager has the ability to bring together all the right resources and organisation to the table to manage the technology to a defined result. Again, as with most successful projects, two-way communication is a requisite in order to perform on track. This spans across multiple disciplines in radiation oncology.

Show clinical efficacy and Return on Investment (ROI)

Most administrative decisionmakers get excited about an initiative if they can understand the value added and can identify with the ROI. The ROI is important for administrators because it can serve as a gauge for/against future performance of technology implementation. A positive ROI can be associated with success. Likewise, evidence-based patient outcomes (lower morbidity and mortality rates, quality of life, etc.) can help sell the technology. The best example is IMRT. We have contributed significantly to the acceptance of IMRT as standard of care in the treatment of various cancers especially head and neck cancers, and prostate cancers. We have shown the clinical efficacy of IMRT on decreasing treatment-related toxicity e.g. xerostomia in head and neck cancer and decreasing rectal toxicity in prostate cancer as well as the improvement in local control. These important achievements have led to a positive impact on ROI as the current return on technical charges has also increased accordingly. Hence, if individuals responsible for technology implementation can see the added value, embracing and buying into the project facilitates successful implementation.

Ability to articulate the project

One of the keys to get a project off the ground is being able to articulate your vision to the decision makers: a one-page summary or a two-minute elevator conversation. Some people say too much, while others do not say enough. It is important for the project champion to be balanced in brevity with verbosity, while hitting the key points. Outcomes, cost, executive support and ROI are key drivers and content areas one should have at the tip of their tongue.

Celebrate Successful Implementation

One of the most authentic ways to recognize successful project implementation is to celebrate with all those who contributed to its success. Handwritten notes to individuals, lunch or dinner meetings, a day off, and public recognition are all great ways to celebrate success. The most rewarding celebration for us is when we are recognised as the pioneers or “gurus” in these innovative approaches. Positive reinforcement goes a long way in establishing strong working relationships with those who contribute to successful implementation.

CONCLUSION

Pioneering and implementing new technology successfully in a radiation oncology clinic are very important endeavors and require hard work, team effort as well as the management support. We have successfully achieved these endeavors in our clinics over the last 15 years, following the five fundamental principles discussed above.

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