Intensity modulated radiotherapy (imrt) in the treatment of malignant tumours

With respect to the localisation, radiotherapy planning and treatment delivery, critically evaluate the role of Intensity Modulated Radiotherapy (IMRT) in the treatment of malignant tumours in the head and neck region.

Introduction

Intensity modulated radiotherapy (IMRT) is a radiotherapy treatment technique which can be used for a multitude of treatment sites. IMRT uses many segments to create one individual treatment field with the objective being to produce a higher conformity than would be achievable with a standard conformal treatment plan. The technique usually involves 5 to 7 beams, each with its own intensity profile, to conform the dose tightly to the target volume allowing normal tissue and critical organs to be spared. The multi leaf collimator (MLC) is controlled by the computer to create these segments (Symonds, Deehan, Mills & Meredith, 2012). IMRT can currently be delivered through either a ‘ Step and shoot’ or a ‘ Sliding window’ technique. The step and shoot technique is simpler and involves segments being delivered at specific angles with the sum of the delivered segments creating the required beam modulation. The sliding window technique utilises a continuously moving MLC with leaves moving at different speeds creating a dynamic beam modulation. Volumetric modulated arc therapy (VMAT) is an expansion on this sliding window technique in which during the treatment the gantry is arced at various speeds delivering the highly-conformed treatment in a shorter time compared to IMRT (Symonds, Deehan, Mills & Meredith, 2012).

The purpose of this essay is to critically evaluate the usefulness of IMRT in the treatment of head and neck region malignant tumours. To do this IMRT's role throughout the patient's radiotherapy pathway must be evaluated. This includes how IMRT influences the localisation and planning of a patient's treatment as well as their treatment and verification. Other important factors to consider is how IMRT allows for the possibility of image fusion as well as its impact on immobilisation.

Discussion

Localisation

IMRT increases the conformity of the treatment to the target volume, this creates a higher risk for a geographical miss to occur. Therefore, enhanced immobilisation is necessary for IMRT treatments. Inaccuracies in target positioning can be reduced effectively with the proper implementation of the correct immobilisation techniques (Saw, Yakoob, Enke, Lau & Ayyangar, 2001). Enhanced immobilisation is additionally important for tumours in the head and neck region due to the close proximity of critical structures as well as the commonly small size of many head and neck tumours. One of the enhanced immobilisation techniques that have been used in clinical practice is thermoplastic shells, made specifically for individual patients during their treatment planning (Arino, Stadelmaier, Dupin, Kantor & Henriques de Figueiredo, 2014). Vac bags are also common in modern patient setups for IMRT treatments as they help to stop the patient moving as well as being a useful indexing tool.

To achieve the dosimetric advantages of IMRT, the localisation and delineation of the tumour and adjacent clinical structures must be accurate. The availability of CT simulators facilitates accurate 3D localisation which is vital to the effectiveness of IMRT. It is important to have 3-dimensional localisation to accurately plan the treatment and capture the full advantage of IMRTs conformity for the entire of the PTV. CT images also have a high spatial integrity and good spatial resolution as well as providing information on electron density required for calculating dose distribution (Cheung, 2006). The high conformity of the treatment allows for dose escalation due to the sparing of the surrounding tissues, therefore the accurate delineation of surrounding structures as well as the target volume is even more important than in conventional radiotherapy.

The development of image fusion software has enabled more accurate contouring than before as multiple modalities can be used to combine the advantages of each. MR images have a superior contrast resolution for soft tissue, making them an extremely useful tool. A study undertaken in 2003 showed that MRI and CT fused images improved the delineation of the target volumes and the organs at risk (OAR) (Emami, Sethi & Petruzzelli, 2003). This study was conducted in 2003 and had a sample size of just 8 patients. The small sample size could suggest a lack of reliability and how valid the information is across the whole of the UK. CT and other imaging modalities have improved since this study was undertaken and so the effectiveness of image fusion could have changed. Positron emission tomography is another imaging modality which enhances the accuracy of contouring for IMRT treatments. A study looking at patients with brain tumours compared CT and

MRI alone to fused CT, MRI and PET enables a more accurate determination of the GTV and PTV (Zelefsky, Fuks & Leibel, 2002).

IMRT itself does not allow for a reduced margin around the target volumes. Instead it is the enhanced verification techniques and increased immobilisation which is required for IMRT treatments. This is an additional advantage of the implementation of IMRT into centres across the UK as it allows for dose escalation to the GTV without exceeding dose constraints for normal tissue and OAR due to the sparing effect produced by having smaller margins (Kron, 2008). Head and neck patients benefit the most from this as the structures in the head and neck region are very close together and with conventional radiotherapy treatment would have received very high doses of radiation.

This sparing effect was highlighted in the PARSPORT trial. This study compared the effectiveness of IMRT to conventional radiotherapy in sparing the parotid gland in head and neck cancers. IMRT was found to have better coverage of the PTV as the volume receiving at least 95% of the prescribed dose was better for all the PTV's included in the study. The left parotid gland received a mean dose of 30. 3 Gy for IMRT treatments whereas the 3D conventional radiotherapy treatment delivered a mean dose of 42. 69 Gy. This data set had a p-value of 0. 0027 and therefore we can reject the null hypothesis that no difference between the means exists and conclude that a significant difference does exist between the two groups. The sample size of this study was relatively small (73 patients being included after 12 months and 55 after 24 months). The methodology for this study is extensive and therefore the reproducibility of the study is high. Since this study was published several small non-randomised studies have supported the conclusions of the PARSPORT trial. It was not possible to mask the treatments from clinicians and patients due to the differences in treatment delivery (Nutting et al., 2011).

IMRT is extremely useful for treating malignancies in the head and neck region, but it is only possible due to the advancements in localisation technique. A centre which has no access to a CT simulator or a patient which is being marked up on set would not benefit greatly from IMRT and it could possibly end up being more detrimental when compared with conventional radiotherapy. Many head and neck patients are palliative and the increased immobilisation may not be suitable for these patients. Some patients find it difficult to tolerate the thermoplastic shells and will either receive treatment with no shell or a much looser mask to reduce the feeling of claustrophobia (Arino, Stadelmaier, Dupin, Kantor & Henriques de Figueiredo, 2014). In these cases, the risk of a geographical miss due to positional inaccuracies could be considered too high and therefore conventional radiotherapy may be a better option.

Planning

The implementation of IMRT brought around a change in treatment planning. IMRT plans are usually created through a process called Inverse planning as opposed to conventional radiotherapy treatments which are created through forward planning. Inverse planning is when a set of dose constraints are created by the planner and entered into an optimisation software on the treatment planning system (TPS) (Bär et al., 2003). The TPS will then create a plan based on these dose constraints and it is up to the planner to tweak these constraints to create the best possible plan. Typical dose constraints for an IMRT plan would include that 99% of the PTV should receive at least 90% of the prescribed dose and 95% should receive 95% of the prescribed dose. Another constraint is that no more than 2% of the volume should receive 107% of the dose and no more than 5% of the volume should receive more than 105% (Symonds, Deehan, Mills & Meredith, 2012).

Forward planning can be used to create some simple IMRT plans, however this is normally used for breast technique. Whilst forward planned IMRT does offer an improvement over a standard treatment plan it does not offer the conformity of inverse planned IMRT treatments for head and neck tumours and therefore centres opt for inverse planning when using IMRT in the head and neck region (Bär et al., 2003).

Whilst inversely planned IMRT offers conformity and dosimetric advantages over forward planning and conventional treatments it is not without its drawbacks. The optimisation software will only attempt to spare areas or volumes which have been completely outlined. This creates the need for pseudo structures. These are used to cover areas which do not have strict dose restraints but the planner does not want hot spots to occur, these areas will be given a low priority in the TPS but the dose constraint should help to reduce overspill of dose. The optimisation algorithm will have to be run multiple times and these structures edited to achieve the optimal plan. This is time consuming for the planner as the optimisation algorithm can take a long time as well as constant editing of dose constraints and pseudo structures. It is also the job of the planner to decide how many beams they want to use, this causes an issue as multiple arrangements must be tried before finding the optimum value which may eventually be unrealistic for clinical use (Deshpande, Sathiyanarayanan, Bhangle, Swamy & Basu, 2007). This is where forward planned IMRT may be more useful if the treatment is simple and patient needs to be treated urgently as the turnaround from localisation to treatment will be much quicker.

The widespread implementation of inverse planning has brought about a change in regulations with the introduction of ICRU 83. ICRU 83 governs the use of inverse planning and has changed how plans are reported. The ICRU 83 report emphasises the use of dose volume histograms (DVH) in prescribing, recording and reporting. The DVH is now a critical tool in the evaluation of complex 3D absorbed dose distributions and even more so for IMRT. The report recommends that dose volume specifications be used for reporting the treatment plan. The median absorbed dose (D50%) should be reported instead of the dose at the ICRU reference point. The median absorbed dose represents the absorbed dose received by 50% of the volume. The reporting of D100% is not recommended and instead the near minimum absorbed dose (D98%) should be reported as it is more reliably determined. The near maximum absorbed dose (D2%) should be reported instead of the maximum absorbed dose which has been previously recommended. This extensive change in reporting procedure requires new software to be developed by centres to abide by these recommendations. This can be costly if the software is bought in or time consuming if it is developed in house. However, the implementation of ICRU 83 has standardised and streamlined the reporting of IMRT plans and has therefore been a very welcome and useful change for IMRT planning (“ The International Commission on Radiation Units and Measurements”, 2010).

The use of IMRT in radiotherapy centres brings a lot of change for the medical physics and planning departments. Centres with a small planning department may opt for forward planned IMRT to reduce the workload and pressure however these are known to not bring the full benefit of IMRT. The amount of time involved in creating an IMRT plan may lead centres to use conventional radiotherapy techniques to treat urgent patients to avoid costly time delays.

Treatment and verification

The importance of image guided radiotherapy (IGRT) is emphasised when using an IMRT treatment plan. Although increased immobilisation techniques aim to combat the possibility of a geographical miss, which the risk of is increased by the tight conformity to the PTV produced by IMRT treatments, there is still the chance of a geographical miss occurring. As immobilisation cannot achieve complete immobility there is still the need for a margin between the CTV – PTV (Symonds, Deehan, Mills & Meredith, 2012). Effective verification of patient positioning achieved by IGRT can reduce this margin using daily and weekly imaging protocols. In the head and neck region these protocols would focus on the bony and soft tissue matches as well as the repositioning of the isocentre (Lewis-Jones, Colley & Gibson, 2016). The use of online imaging and positioning correction prior to treatment delivery facilitates a reduction in this CTV – PTV margin. Daily imaging however can increase the time spent in the department by patients by lengthening their treatment times as well as the possibility of causing delays for other patients.

The use of kV images for the online verification of head and neck patients is a standard protocol. MV images are not often used for the head and neck region as there are a large number of structures in the head and MV images are not of a good enough quality for a reliable and accurate match to be made. Images produced using kV x-rays allow for the matching of bony anatomy but does not provide sufficient depth of positional information for a soft tissue match to be completed. Therefore, centres may use weekly or daily cone beam computed tomography (CBCT) to achieve a soft tissue match. CBCT is especially effective for the verification of head and neck tumours as these patients often experience weight loss during treatment and the patients outline is captured well during a CBCT. This can help to suggest whether changes in immobilisation may be useful to reduce the risk of systematic errors further than what daily imaging protocols already do (Leech et al., 2017).

The minimisation of the CTV – PTV margin can reduce the dose absorbed by the surrounding structures of the head and neck region, of which there are many. Daily IGRT does however increase the dose received by the patient throughout their entire treatment. The dose received by patients over treatment usually equates to 0. 1% to 3% of the total treatment dose, this is insignificant when compared to the benefits of effective IGRT in head and neck cancer management.

Conclusion

The use of effective IGRT combined with enhanced immobilisation techniques is vital in ensuring the clinical confidence in the practice of advanced radiotherapy techniques such as IMRT. The accurate delineation of treatment volumes and OAR is extremely important for the planning process of IMRT as well as the overall effectiveness of the patient's treatment. Without correct determination of critical structures positions the dose sparing and dose escalating benefits of IMRT would become a negative in the patient's treatment. IMRT has been shown to help reduce the side effects of radiotherapy treatment for patients when compared with standard 3D conformal treatments (Bär et al., 2003). IMRT is extremely advantageous for head and neck cancers due to the proximity of critical structures in the region as well as the low tolerance doses of the OAR in the area.

It can be concluded that IMRT plays a vital role in the management of head and neck cancers for most tumour sites. The high conformity of IMRT reduces dose delivered to OAR and healthy surrounding tissue whilst giving the ability to escalate dose to the GTV. Despite this a standard conformal radiotherapy treatment may still be the best option for palliative patients receiving a simple plan as well as for patients requiring urgent treatments. Centres without the access to advanced planning systems and quality assurance systems, particularly in less developed countries, may find it difficult to implement IMRT. IMRT has changed how head and neck tumours are managed and has changed the outcome for the patients undertaking treatment.

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