Advances in Head-and-Neck Interventional Radiotherapy (Brachytherapy)

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Interventional radiotherapy, also known as brachytherapy, is the use of sealed radioactive sources that directly deliver radiation to the tumor or tumor bed. Its unique dose distribution profile allows for high conformality, making it a very useful modality in the treatment of cancers in the head and neck, where different organs and substructures that serve various but related functions are situated close to each other.

In recent years, we have seen several important technological breakthroughs in the field, especially regarding its application in head and neck cancers. These include advances in *treatment delivery, dosimetry planning*, *image guidance*, and *catheter positioning techniques*. These innovations, which often require interdisciplinary interventions, have resulted in enhanced treatment accuracy, and therefore, major clinical advantages in terms of increased local control and decreased toxicity, as well as economic benefits.

In order to highlight the differences from old brachytherapy techniques, a more appropriate terminology should perhaps be adopted, to signify these advancements that resulted in new opportunities, approaches and better outcomes – interventional radiotherapy (IRT). Such a change in terminology will not only allow recognition of these advances, but also a meaningful distinction from obsolete techniques and suboptimal outcomes that are associated with traditional brachytherapy. This is very important in increasing awareness among professionals outside the field of radiation oncology.

We briefly review these recent advances, the current indications, and future directions for IRT in head-and-neck cancers.

Technological and Technical Evolutions

Dosimetry planning and treatment delivery. A significant contribution to the evolution of IRT has come from the industry through the development of sophisticated remote afterloading machines, advanced treatment planning software and high-technology applicators that are increasingly smaller, easier to handle and are MRI- and CT-compatible. In contrast to traditional techniques that entail direct handling implantation of radioactive wires, remote afterloading entails robotic manipulation of a radioactive seed source through implanted inert catheters or applicators. Direct handling

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of radioactive wires exposes the implanting physician, and the geometry of wires limit the dose optimization. The use of inert implantation materials improves personnel radiation safety and allows for greater optimization during implantation. The use of robotic manipulation of the radioactive seed source allows for greater optimization of dose distribution by designating dwelling points and dwelling times along the course of the implanted inert catheters.[1]*Image guidance.* Traditional approaches relied on defined dose geometry prediction systems to guide implant and dosimetry planning. Coupling the above advancements with three-dimensional imaging, more accurate target volume and organ-at-risk delineation and volumetric dose distribution estimation could now be achieved, called image-guided interventional radiotherapy (IG-IRT).

Image guidance would allow for safe dose-escalation and dose-modulation to tumor sub-volumes, called intensity-modulated interventional radiotherapy (IM-IRT). Additional anatomic and functional information from different imaging modalities such as magnetic resonance imaging (MRI) and positron emission tomography (PET) could guide personalization of dose distribution.

Advanced treatment planning systems. Advanced treatment planning systems (TPS) integrate dose calculation algorithm that accounts for density inhomogeneities between tissues, allowing for more accurate dose estimation. These systems allow for part or full automatization of the different processes such as image fusion or image co-registration, digital reconstruction of catheters or applicators, and calculation of biological equivalent doses.

Image fusion allows direct superposition of multiple image sets such as MRI or PET into a reference image set, usually the computed tomography simulation scan, allowing for more accurate and precise volume delineation, compared to comparing image sets side-by-side.

Automated digital reconstruction of catheters and applicators facilitate and enhance that accuracy of the reconstruction process by using a set of digital libraries or representations of rigid catheters and libraries. This is important because dosimetry planning is based on the assumption that radioactive source channels are mapped accurately.

Automated calculation of biological effective doses incorporates formulas for conversion of physical to biological doses and allows the physicist to optimize dose distribution according to biological, rather than physical doses (biological planning). The preliminary data on the use of biological planning in IRT are promising but further validation would be required.

The need for complex IG-IRT modalities has stimulated research in the radiobiological field on the effectiveness and safety of increasingly more hypofractioned radiotherapy protocols. Hypofractionation entails delivery of the total treatment dose over fewer, but higher-dose fractions, allowing for shorter overall treatment times and better patient comfort and convenience.

Catheter-Positioning Techniques

Traditionally the catheter implant has been performed using the Paris rules system, which implies a geometrical disposition of needles or plastic tubes. Such disposition is based on a well-defined disposition on several layers that by respecting a fixed distance among the catheters allows to adequately cover treatment volumes of different sizes. In particular, such system permits to reach an optimal dose distribution within the treatment volumes avoiding excessive dose inhomogeneities.

Typical examples of catheter implants performed according to the Paris system include tongue[2] and lip cancer.[3]More recently a different concept has been proposed in the context of nasal vestibules, that is the anatomical implant. Such an approach is sustained by the rationale to respect anatomical planes avoiding piercing the perichondrium, in fact, perichondrium integrity is a major factor in prevention of septal perforation.[4]

Current Indications

The above developments bring great promise to the future applications for IRT in head-and-neck cancers. Given the current evidence with the use of these technologies and techniques, we can identify some scenarios in which the use of IRT could be useful:

1. IRT boost integrated with external beam radiotherapy for dose escalation;

2. Postoperative IRT in case of unexpected positive surgical margins;
3. Re-irradiation (IRT alone, or postoperative IRT); and
4. IRT alone.

Regarding the last point, the use of exclusive, definitive IRT is gaining more usage under the paradigm of "surviving is not enough". Indeed, especially for head-and-neck skin cancer, nasal vestibule cancer, lip cancer and eye melanoma (using plaque radiotherapy), IRT can offer not only excellent local control but also aesthetic and functional outcomes, and therefore good quality of life. In these scenarios, patient values and preferences should be considered and IRT offered as a valid alternative to more radical surgical approaches.

Emerging Advancements

The next big developments in IRT will likely come from the introduction of artificial intelligence. Big-data analysis using large databases and machine-learning or neural networks to inform patient selection for IRT to develop predictive models, and thus develop useful decision support tools. Moreover, IRT requires quality assurance and training due to its technological complexity. The introduction of the artificial intelligence-guided procedure (AIGP) and automation in clinical practice could be very useful. The impact of this introduction will not be negligible and could improve all phases of the IRT workflow.[5]

CONCLUSION

The evidence and advances highlighted in this article are encouraging about the use of IRT in head and neck treatment, with the aim to improve both the prognosis and quality of life of patients.

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