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Intensity-modulated radiotherapy for paranasal sinuses and base of skull tumors

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ABSTRACT

Paranasal sinus and skull base tumors are rare aggressive head and neck cancers, and typically present in the locally advanced stages. As a result, achieving wide surgical resection with clear margins is a challenge for these tumors, and radiotherapy is thus usually indicated as an adjuvant modality following surgery to optimize local control. Given the integral role of radiotherapy in the management of this subgroup of head and neck tumors, the advent of intensity-modulated radiotherapy (IMRT) has led to substantial improvement of clinical outcomes for these patients. This is primarily driven by the improvement in radiation dosimetry with IMRT compared to conventional two dimensional (2D)- and 3D-techniques, in terms of ensuring dose intensity to the tumor target coupled with minimizing dose exposure to critical organs. Consequently, the evident clinical benefits of IMRT have been in reduction of normal tissue toxicities, ranging from critical neurological symptoms to less debilitating but bothersome symptoms of eye infections and radiation-induced skin changes. Another domain where IMRT has potential clinical utility is in the management of a subset of non-resectable T4 paranasal sinus and skull base tumors. For these inoperable lesions, the steep dose-gradient between tumor and normal tissue is even more advantageous, given the crucial need to maintain dose intensity to the tumor. Innovative strategies in this space also include the use of induction chemotherapy for patient selection. In this review, we summarized the data for the aforementioned topics, including specific discussions on the different histologic subtypes of paranasal sinus and skull base tumors.

Introduction

Cancers of paranasal sinus and skull base are uncommon, and constitute only a small proportion of all head and neck malignancies [1,2]. The maxillary and ethmoid sinuses comprise the most frequent sites of origin. However, these tumors can be histologically diverse; squamous cell carcinomas comprise about half of all cases, with adenoid cystic-, mucoepidermoid-, sinonasal undifferentiated- and adenocarcinoma, esthesioneuroblastoma, melanoma and chordoma variants making up the remainder [3,4]. In terms of clinical presentation, tumors in the paranasal sinuses are relatively asymptomatic as they occur in large air cavities, and therefore patients often present with advanced disease when the tumors involve the adjacent critical normal structures like the orbits, optic pathways and skull base. It is for this reason that treatment of paranasal sinus tumors is often complex, requiring a multidisciplinary team approach. Consistent with the broad principle of management of head and neck cancers, surgical resection with wide margins is the preferred treatment modality for first-line therapy. Nonetheless, this can be a challenge given the close proximity to delicate normal organs and the restricted anatomical boundaries at the orbit, cranium, skull base, and parapharyngeal spaces. As a result, adjuvant radiotherapy is nearly always indicated to target macroscopic or occult microscopic disease following surgery. Likewise to surgery, there are several considerations when delivering radiotherapy, ranging from tissue in homogeneity (contributed by large air gaps post-surgery), significant anatomical variation post-surgery, ensuring adequate dose intensity to the surgical bed, and importantly, limiting normal tissue toxicities. These issues are now better circumvented by the technical

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advancement of intensity-modulated radiotherapy (IMRT), given the wider degree of flexibility to conform radiotherapy doses and ensuring steep dose gradients at crucial tumor-normal tissue interphase. In this review, we will provide a background to the tumor targeting and technical concepts of radiotherapy for paranasal sinus and skull base tumors; focus on the clinical evidence supporting the advantages of IMRT and the utility of IMRT for each histological subtype; and lastly, we will highlight some of the upcoming potential advances in treatment for these tumors.

Search strategies and outcome

We searched the PubMed, MEDLINE and EMBASE databases for articles published in English before June 1, 2018, with the keywords: “paranasal sinus”, “sinonasal”, “sinus”, “skull base”, “radiotherapy”, “adjuvant”, “postoperative radiotherapy”, “radical”, and “intensity-modulated radiotherapy”. Priority was accorded to original research articles focusing on radiotherapy role in the treatment of paranasal and skull base cancers. Selected references were judged on relevance, and included widely referenced and highly regarded older seminal work. We identified 20 clinical studies that matched the above criteria, which comprised of nine retrospective studies reporting on outcomes of radical and adjuvant radiotherapy [5–13], and eleven studies comparing outcomes using conventional radiotherapy and IMRT [14–24] (Fig. 1).

Radiotherapy tumor target concepts

Target volume delineation and prescribed radiotherapy doses

In the post-operative setting, residual gross tumor volume (GTV) and the pre-operative GTV using co-registered pre-operative computed tomography (CT) and/or magnetic resonance imaging (MRI) datasets should be outlined. This process should be performed taking into account the details of the operative procedure and surgical histopathology report, so that the pre-surgery tumor extent and subclinical tumor spread are comprehensively included into the clinical target volume (CTV). Additionally, the post-operative CTV includes the resection cavity, and the immediate adjacent paranasal/anatomical compartments, regardless of involvement. For example in a maxillary sinus tumor, this would include the adjacent ipsilateral nasal cavity, nasopharynx, ethmoid and sphenoid sinuses (Table 1). In special instances where the tumor extends intracranially, and a craniofacial resection is performed, the dural bed with a 0.5–1 cm margin ought to be included in the CTV. Separately, in adenoid cystic carcinoma of the paranasal sinuses, the CTV should also include the involved nerve(s), tracked from the tumor region to the base of skull. For non-resectable tumors, CTV delineation largely follows the principles outlined for the post-operative cases, but also includes a circumferential 5- and 10-mm expansion margin around the intact primary GTV, taking into account anatomical boundaries.

Radiotherapy dose prescription patterns are largely consistent across institutions, and vary by clinical scenarios. 60 Gy and 66 Gy are typically employed for microscopic disease in the adjuvant setting, with the latter higher dose being reserved for cases with high-risk features

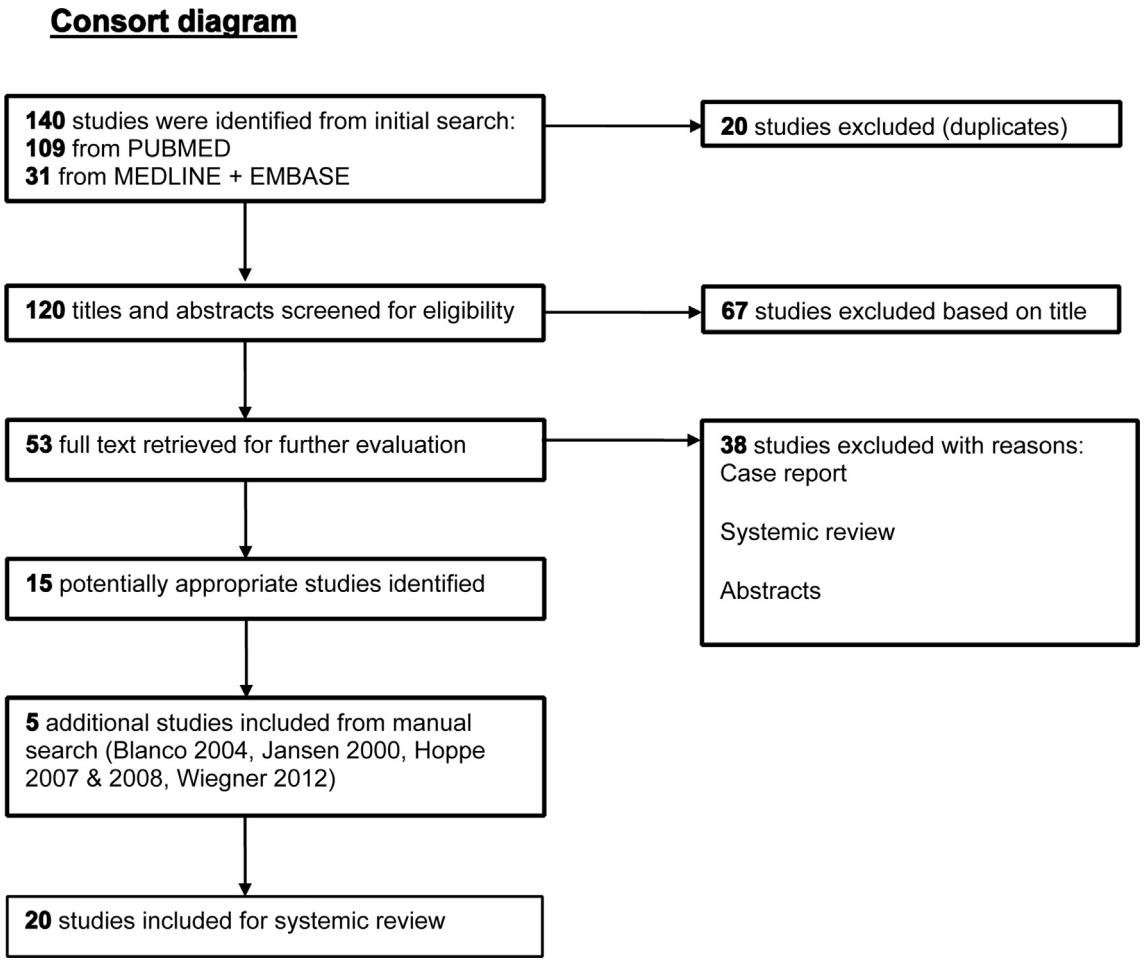

Fig. 1. Selection process for studies reporting on outcomes of radical and adjuvant radiotherapy for patients with paranasal sinus tumors.