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Review Article

An Evidence-Based Review of Total Body Irradiation

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ABSTRACT

The purpose of this literature review is to investigate clinical treatment methods of total body irradiation within the context of a clinical department adopting a paediatric cohort with no existing technique. An extensive review of the literature was conducted using PubMed, Science Direct, Google Scholar, and Clinicians Knowledge Network. Articles were limited to nonhelical tomotherapy, nonparticle therapies, and those using hyperfractionated regimes. Total marrow irradiation was excluded because of national treatment and trial limitations. Of the numerous patient positioning methods present within the literature, the most comfortable and reproducible positioning methods for total body irradiation include both supine and the supine and/or prone combination. These positions increased stability and patient comfort during treatment, while also facilitating computed tomography data acquisition at the simulation stage. Ideally, dose calculations should be performed using a three-dimensional treatment planning system and quality assurance procedures that include in vivo dosimetry measurements. The available literature also suggests inhomogeneity correction factors and intensity modulation are superior to conventional open field techniques and should be implemented within developing protocols. Dynamic machine dose modulation is suggested to reduce department impact, removing the need for tissue compensators and accessory shielding devices, while providing significant improvements to treatment time and dose accuracy. Further long-term survival and intensity modulation studies are warranted, including direct comparisons of both dose modulation and treatment efficiency.

RÉSUMÉ

Cette recherche documentaire vise à examiner les méthodes de traitement clinique d'irradiation corporelle totale (ICT) dans le contexte d'un service clinique adoptant une cohorte pédiatrique sans technique existante.

Une recherche documentaire approfondie a été menée dans Pubmed, Science Direct, Google Scholar et Clinicians Knowledge Network. La recherche a été limitée à la tomothérapie non hélicoïdale, aux thérapies non particulaires et aux thérapies faisant appel à des régimes d'hyperfractionnement. L'irradiation totale de la moelle osseuse (ITM) a été exclue en raison des limites associées au traitement national et aux essais.

Parmi les nombreuses méthodes de positionnement du patient présentées dans les études, les plus confortables et reproductibles pour l'ICT sont la position couchée sur le dos et la combinaison de position couchée sur le dos et le ventre. Ces positions permettent d'augmenter la stabilité et le confort du patient durant le traitement tout en facilitant l'acquisition des données de TDM à l'étape de la simulation. Idéalement, le calcul de la dose devrait être fait en utilisant un système de planification du traitement en trois dimensions Ainsi que des procédures d'assurance de la qualité comprenant des mesures de dosimétrie *in-vivo*.

La documentation scientifique disponible suggère également que les facteurs de correction de l'inhomogénéité et la modulation d'intensité sont supérieurs aux techniques conventionnelles de champ ouvert et devraient être mis en œuvre dans les protocoles en développement. Il est suggéré de recourir à la modulation dynamique mécanique de la dose, ce qui permet de réduire l'incidence sur le service, d'éliminer le besoin de compensateurs de tissus et dispositifs de protection accessoires tout en assurant une amélioration marquée du temps de traitement et de l'exactitude de la dose. D'autres études à long terme sur la survie et la modulation d'intensité sont nécessaires, incluant des comparaisons directes de la modulation de dose et de l'efficacité du traitement.

Keywords: Radiation Therapy; total body irradiation; oncology; bone marrow transplant; stem cell transplant; external beam radiation therapy; paediatric

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Introduction

Over the past 30 years, total body irradiation (TBI) has become an integral part of haematologic stem cell transplant (HSCT) or bone marrow transplant (BMT) preparative regimes [1–3]. HSCT protocols have been developed to focus on the treatment of a variety of oncologic, immunologic, or haematologic diseases, including primarily acute leukaemias, non-Hodgkin lymphoma, and aplastic anaemia [4–6]. Although HSCT was originally designed for the treatment of palliative lymphoma patients in the 1970s, utilisation has become increasingly popular because of the benefit of myeloablative effects on patients and increased radiosensitivity of these diseases [3].

In initial clinical protocols, TBI was given as a single dose of 8 to 12 Gy; with 1-year mortality rates as high as 83% and numerous short-term complications, fractionated treatment was introduced to promote biological recovery and decrease fatalities [7, 8]. The target volume of TBI includes all bone marrow cell populations and focuses on ablating these to achieve an immunosuppressant effect. Traditionally, protocols focus on the use of high-dose chemotherapy regimes in conjunction with TBI to reduce or clear the patient's immunity in preparation for transplantation, reducing the risk of transplant rejection or graft versus host disease (GVHD) [9]. With regard to prescriptions, treatment regimens include TBI after chemotherapy to a reference dose (RD), with a homogenous distribution to the entire body target volume, conventionally to within 10% of the RD [10, 11]. Unfortunately, TBI's myeloablation causes cytotoxicity to healthy tissues, necessitating planned dose avoidance to organ structures to reduce complications [12]. To achieve these treatment volumes, the use of large fields and extended distances from the radiation sources are required.

Collectively, there is little evidence of best practice with regard to the development and rationale for varying TBI protocols. Between institutions, the methods and approaches to TBI as a treatment technique vary significantly. The development of this technique requires the use of the multidisciplinary team within a clinical department to establish common goals and interests. The aim of this review was to investigate the literature for evidence of TBI treatment techniques to determine available methods of delivery for use within a department with no current TBI technique.

Methods

Literature Selection Criteria

An extensive review of the literature was conducted to gather evidence of TBI approaches, to determine a suitable technique for implementation or modification. This review was conducted using search terms within PubMed, Science Direct, Google Scholar, and Clinicians Knowledge Network. Inclusion criteria for review included radical TBI treatments delivered with external beam radiotherapy (EBRT) photons to both adults and children.

Total marrow irradiation (TMI) therapies were excluded from results because of a lack of use within Australia. In addition, helical tomotherapy, radioactive sources, and particle modalities were also excluded because of departmental equipment limitations. Finally, single fraction regimes were excluded because of the age of clinical data and current biological understandings, which restricted the articles to post-1980.

Results

Approximately 120 articles were reviewed based on their abstracts, of which 88 articles met the inclusion criteria after full review. Four key components of the TBI technique were identified from the literature. These were patient position for treatment, quality assurance (QA) of treatment delivery, planning considerations and constraints, and finally beam modification, technology used, and equipment associated with these techniques. Each of these components has been investigated individually to assess findings present within the literature.

Patient Position

Because of the vast disparity of TBI treatment techniques, technology, and physical limitations of clinical departments, patient positioning has become a major discussion point of TBI treatment technique. Within the investigated literature, 43 original research articles were identified with a description of a treatment technique. As seen in Table 1, the most prevalent patient positions included "supine only" and "supine/prone" orientations. In addition, "other" was defined as not fulfilling the criteria of the remaining positions, or if more than one position criteria was used for the overall treatment delivery.

For patients with previous chemotherapy conditioning present for TBI treatment planning, common complaints included fatigue, nausea, and muscle weakness. This can be further increased because the time-intensive nature of TBI procedures [16].

Multiple sources preferred the orientation of supine positioning. This increased comfort to the patients because they were not required to support their own weight. This anatomic orientation was favoured for clinical departments using three-dimensional dose verification and lateral treatment field techniques [17, 24].

Supine/prone positions followed in popularity, allowing patients to be positioned underneath the treatment gantry

Table 1
Patient Positioning Technique Outlined in Each Article

Patient positioning (43 articles)
Supine only [12–23]
Supine/prone [24–34]
Standing/seated [1, 7, 35–41]
Semi-incline [42, 43]
Lateral decubitus [3, 44–46]
Other [2, 47–49]
Not specified [50]