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Radiation Therapy (RT) Target Volume Definition for Peripheral Primitive Neuroectodermal Tumor (PPNET) by Use of Multimodality Imaging: An Original Article

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Abbreviations: PNET: Primitive Neuroectodermal Tumor; RT: Radiation Therapy; MRI: Magnetic Resonance Imaging; CT: Computed Tomography; PPNET: Peripheral Primitive Neuroectodermal Tumor; IMRT: Intensity Modulated Radiation Therapy; IGRT: Image Guided Radiation Therapy; BART: Breathing Adapted Radiation Therapy; ART: Adaptive Radiation Therapy; LINAC: Linear Accelerator

ABSTRACT

Objective: Primitive neuroectodermal tumor (PNET) refers to a group of highly malignant tumors consisting of small round cells of neuroectodermal origin which may be subdivided into central or peripheral PNET (PPNET) types. Radiation therapy (RT) has been used as part of multimodality management to improve treatment results, however, radiation induced toxicities remain to be critical concerns particularly for pediatric patients with PPNET. In this original research article, we evaluated RT target volume definition for PPNET by use of multimodality imaging.

Materials and Methods: RT target volume definition for PPNET with multimodality imaging by incorporation of magnetic resonance imaging (MRI) or by computed tomography (CT)-simulation images only has been assessed for patients receiving RT for PPNET.

Results: Ground truth target volume serving as the reference for actual treatment and for comparison purposes has been meticulously defined by the board certified radiation oncologists following comprehensive evaluation, colleague peer review, collaboration, and consensus. A group of experts from radiology, surgery, medical and radiation oncology departments have decided for individualized patient management after thorough multidisciplinary assessment. Synergy (Elekta, UK) LINAC has been utilized for irradiation. RT target volume definition with CT only and with incorporation of CT-MR fusion has been assessed comparatively. As the primary result of this study, ground truth target volume has been found to be identical with target volume determination with CT-MR fusion based imaging.

Conclusion: Multimodality imaging with incorporation of MRI in the target definition process may be considered for improving the accuracy and precision despite the need for further supporting evidence.

Keywords: Peripheral Primitive Neuroectodermal Tumor (PPNET); Radiation Therapy (RT); Magnetic Resonance Imaging (MRI)

Introduction

Primitive neuroectodermal tumor (PNET) refers to a group of highly malignant tumors consisting of small round cells of neuroectodermal origin which may affect both soft tissues and bones and these rare but aggressive variant of small round cell carcinomas typically arising from the neural crest cells may be subdivided into central or peripheral PNET (PPNET) types [1-5]. Patients with PPNET may suffer from several symptoms depending on lesion size, localization and association with critical structures. No standardized guideline exists for management of PPNET partly due to the rarity of cases arising in different body sites, however,

multimodal treatment may be utilized as in Ewing sarcoma family of tumors [1-5]. Within this context, surgery, systemic treatments and radiation therapy (RT) may be included in combined modality management of PPNET to achieve improved therapeutic outcomes [1-5]. Despite intensive management, these tumors may typically follow an aggressive disease course with distant metastases in a considerable proportion of patients.

RT has been used as part of multimodality management to improve treatment results, however, radiation induced toxicities remain to be critical concerns particularly for pediatric patients with PPNET. To this end, there has been extensive effort to improve the toxicity profile of radiation delivery to achieve better functionality and quality of life. Precise, accurate, and focused treatment techniques have been developed to improve sparing of critical structures and surrounding normal tissues while effectively irradiating the target volumes. In the context of radiation oncology discipline, there have been substantial progress in recent years with tremendous advances by introduction of adaptive irradiation strategies and modernized treatment delivery techniques with incorporation of Intensity Modulated Radiation Therapy (IMRT), Image Guided Radiation Therapy (IGRT), Breathing Adapted Radiation Therapy (BART), Adaptive Radiation Therapy (ART), automatic segmentation methods, molecular imaging techniques and stereotactic irradiation strategies [6-41]. In this original research article, we evaluated RT target volume definition for PPNET by use of multimodality imaging.

Materials and Methods

RT target volume definition for PPNET with multimodality imaging by incorporation of magnetic resonance imaging (MRI) or by computed tomography (CT)-simulation images only has been assessed for patients receiving RT for PPNET. Ground truth target volumes which served as reference for actual treatment and for comparison purposes have been determined by the board certified radiation oncologists following comprehensive evaluation, colleague peer review, collaboration, and consensus. Comprehensive patient evaluation has been performed with consideration of lesion size and localization, symptomatology, logistical issues, and expected outcomes of treatment. A group of experts including radiologists, surgeons, medical and radiation oncologists have decided for individualized patient management after thorough multidisciplinary assessment. RT simulation has been performed at CT-simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK) available at our tertiary cancer center. Planning CT images have been acquired and then transferred to the delineation workstation (SimMD, GE, UK) for contouring of treatment volumes and nearby critical structures. Either CT-simulation images only or fused CT and MR images have been used for the purpose of RT target volume definition. Treatment planning objectives included adequate target coverage with minimal exposure of surrounding normal tissues. Target volumes determined by CT only and with incorporation of CT-MR fusion have been assessed comparatively. Treatment delivery has been accomplished by use of Synergy (Elekta, UK) linear accelerator (LINAC) with routine incorporation of IGRT by electronic portal imaging and kilovoltage cone beam CT.

Results

Treatment planning has been acomplished by using the available treatment planning systems at our department with the primary objectives of adequate target coverage with minimal exposure of normal tissues for improving the therapeutic ratio. Ground truth target volume serving as the reference for actual treatment and for comparison purposes has been meticulously defined by the board certified radiation oncologists following comprehensive evaluation, colleague peer review, collaboration, and consensus. A group of experts from radiology, surgery, medical and radiation oncology departments have decided for individualized patient management after thorough multidisciplinary assessment. Synergy (Elekta, UK) LINAC has been utilized for irradiation. RT target volume definition with CT only and with incorporation of CT-MR fusion has been assessed comparatively. As the primary result of this study, ground truth target volume has been found to be identical with target volume determination with CT-MR fusion based imaging.

Discussion

Although PPNET is relatively rare, it may cause severe symptoms warranting prompt management. Symptoms may vary depending on lesion size, localization and association with critical structures. Multidisciplinary management of PPNET has typically been derived from Ewing family of tumors. Surgery, systemic treatment, and RT has been included in multidisciplinary management. However, an aggressive disease course may be observed in a considerable proportion of patients with PPNET despite intensive therapies. RT has been utilized as part of multidisciplinary treatment approaches, however, adverse effects of irradiation constitute major concerns particularly for pediatric patients with PPNET. Besides achieving disease control, pertinent aspects of contemporary patient management include preservation of functionality with improved toxicity profile of delivered therapies.

Adverse effects of irradiation may be severe in some patients leading to deterioration in quality of life and functionality. In this context, every effort should be spent to improve the toxicity profile of radiation delivery. Contemporary radiotherapeutic approaches allow for progress in management with irradiation, however, there is room for further achievements to improve the therapeutic ratio. Target definition composes a critical aspect of radiotherapeutic management of PPNET. While RT planning has been typically based on CT simulation of the patients in treatment position, incorporation of data from multimodality imaging may add to the accuracy and precision of target definition process. Generation of

larger than actual treatment volumes should not be considered as a feasible solution to geographic misses since this may significantly increase exposure of normal tissues in close vicinity of the tumor which may lead to excessive toxicity.

On the other hand, generation of smaller than actual volumes should also be discouraged since it may result in inadequate target coverage with subsequent treatment failures. From this prospect, accuracy and precision in target definition are indispensable components of successful PPNET management. Combined use of CT and MR images may significantly improve target definition for accurate and precise irradiation of PPNET. Several other studies have also addressed incorporation of multimodality imaging for RT target determination [42-68]. Admittedly, determination of the ground truth target volume may be prone to variations due to possible interobserver variations. In this study, board certified radiation oncologists have performed the definition of ground truth target volumes following detailed evaluation, colleague peer review, collaboration, and consensus to achieve optimal results. Our study may add to the growing body of literature by supporting the utility of multimodality imaging for accurate and precise target volume definition for PPNET.

Conclusion

In conclusion, multimodality imaging with incorporation of MRI in the target definition process may be considered for improving the accuracy and precision despite the need for further supporting evidence.

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