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DOSIMETRIC COMPARISON BETWEEN IMRT AND 3D-CRT TECHNIQUES IN POSTSURGICAL RADIOTHERAPY OF A PLEOMORF LIPOSARCOMA OF THE THIGH

BY

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Abstract. Pleomorphic liposarcoma represents approximately 5% to 15% of all liposarcomas and it is much more aggressive than other liposarcoma subtypes and highly resistant to conventional treatment. Radiotherapy was associated with improved overall survival compared with surgery alone. We present the case of a 74year-old patient, diagnosed with pleomorphic liposarcoma, who after complete healing from surgery, was guided to the radiotherapy department where he received postoperative radiotherapy at a total dose of 66Gy/33fr. The technique chosen was intensity-modulated radiotherapy, after a dosimetric comparison between intensity-modulated radiotherapy and three-dimensional conformal radiation therapy techniques was performed on the same tumor volume. The use of new radiation techniques, like intensity-modulated radiotherapy has improved quality of life and dose localizations, increasing local control and disease-free survival and at the same time a decrease in early and late effects of radiotherapy including bone fractures, oedema and joint stiffness.

Keywords: pleomorphic liposarcoma; radiotherapy; intensity-modulated radiotherapy; three-dimensional conformal radiation therapy; dosimetry.

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1. Introduction

Liposarcoma (LPS) is the most common soft tissue sarcoma (STS) (Nassif *et al*., 2016), accounting for approximately 20% to 25% of all STS (Hui, 2016). Pleomorphic liposarcoma (PLS) represents approximately 5% to 15% of all liposarcomas and it is much more aggressive than other LPS subtypes and highly resistant to conventional treatment (Peng *et al*., 2017). PLS is a clinically, histologically and cytogenetically distinct form of liposarcoma and is the rarest subtype, it can occur in lower limbs, mediastinum, liver, orbit, para-testicular region and also as a pure dermal tumor (Bathla *et al*., 2013).

Complete surgical resection is the main local disease treatment method. Radiotheraphy (RT) and conventional cytotoxic chemotherapy remain controversial for metastatic or unresectable LPS (Peng *et al*., 2017).

Radiotherapy was associated with improved overall survival compared with surgery alone when delivered as either preoperative radiotherapy or postoperative radiotherapy (Nussbaum *et al*., 2016).

2. Case Report

We present the case of a 74 year-old patient with multiple cardiovascular pathological antecedents who presented herself in the surgery service in June 2015, claiming the appearance of a tumor on the anterior-medial face of the right thigh, declaring an evolution of about 7 months.

After performing an ultrasound guided puncture, whose anatomo-pathological outcome confirmed the presence of a sarcoma like tumor, the patient underwent an MRI examination. The exam highlighted a large 131/66/71 mm tumor formation in contact with the cortical bone encompassing the femoral vasculo-nerve package on the right thigh. Subsequently, she underwent surgery for excision of the tumor.

The anatomo-pathological outcome confirmed the presence of a pleomorphic grade II liposarcoma (FNCLCC) pT2bNx-G2, R1 resection. After complete healing, the patient was guided to the radiotherapy department where he received postoperative radiotherapy at a total dose of 66Gy/33fr.

The technique chosen was intensity-modulated RT (IMRT), after a dosimetric comparison between IMRT and three-dimensional conformal radiation therapy (3D CRT) techniques was performed on the same tumor volume.

3. Materials and Methods

The patient was simulated with CT-Simulator Siemens Somatom Definition AS, lower extremities protocol, 3 mm slices thickness, in the dorsal decubitus position, and the isocentre was established at the pelvic level (the anatomical projection of the great left and right trochanter and pubic

symphysis). We also fixed a metal wire on the postoperative scar. The treatment plan was performed in Eclipse 11 Treatment Planning. After performing a fusion between preoperative diagnostic images and those obtained at simulation, the gross tumor volume (GTV) preoperative volume was outlined. The clinical target volume 66 (CTV66) should encompass the entire GTV preoperative and immediate area of surgical disruption + 1 to 2 cm margin in the longitudinal plane + 1.5 cm margin in the transverse plane. This may, but not always, include all surgically disturbed tissues, scars, and drain sites, which may be included in a wider subclinical elective volume (Nancy *et al*., 2015). To create the planning target volume (PTV) we expanded the CTV66 by adding +0.5 cm margin.

The outlined risk organs were: left and right femoral head, bladder, rectum, vagina, left and right labia, according to RTOG (Fig. 1).

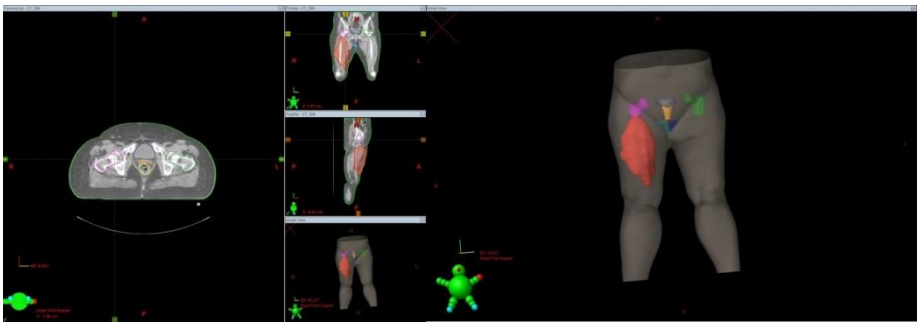

Fig. 1 – The contoured OAR and PTV.

In the thigh sarcoma RT, vulva (vagina + labia) is not defined as a OAR, but its contouring and dosimetric constraints application can reduce the risk of overdosage by inverse planning when treatment planning systems (TPS) randomly chooses beam orientation. Studies on gynecological cancers have shown the risk of vaginal stenosis with implications for quality of life in radio-treated patients with external beam irradiation followed by brachytherapy (Morris *et al*., 2017).

Daily kilovoltage image-guidance (Kv) was used in checking the position of the patient. The treatment was carried out with Varian Clinac iX 10MV.

4. Results

For a dosimetric observation, two treatment plans were created on the PTV volume: IMRT and 3D-CRT (Fig. 2).

After analyzing the dose-volume histogram (DVH), we obtained radiation dose data received by the organs at risk throughout the two techniques. Through the 3D-CRT technique, we obtained these values: vagina maximum dose 12.94Gy mean dose 6.686Gy, left labia maximum dose 16.90Gy mean

dose 12.01Gy, right labia maximum dose 39.73Gy mean dose 15.68Gy, right femoral head maximum dose 63.44Gy mean dose 18.85Gy, left femoral head maximum dose 6.68Gy mean dose 3.39Gy. And through IMRT technique, we obtained these values: vagina maximum dose 10.49Gy mean dose 2.47Gy, left labia maximum dose 9.92Gy mean dose 7.87Gy, right labia maximum dose 19.18Gy mean dose 10.89Gy, right femoral head maximum dose 66.49Gy mean dose 9.81Gy, left femoral head maximum dose 4.72Gy mean dose 1.53Gy. The conformity index (CI) for 3D-CRT was 1.1 and for IMRT 0.6.

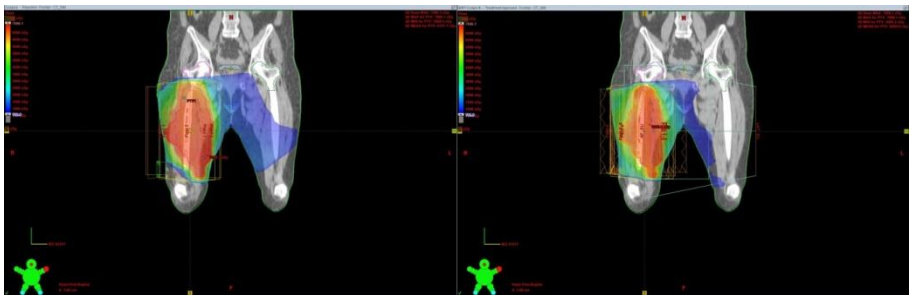

Fig. 2 – Color wash dose-volume histogramcomparison between 3D-CRT(left) and IMRT (right).

5. Discussions

Adjuvant radiation therapy has been demonstrated to provide improved local control (LC) for STS of the extremity following limb-sparing surgery, and may be administered via brachytherapy or external-beam RT (EBRT). Many EBRT options exist, including conventional EBRT, IMRT and other advanced techniques including proton therapy (Folkert *et al*., 2014). Dose conformality is especially important for large tumors such as sarcoma, providing adequate coverage of the periphery, and homogeneous coverage ensures that all tumor cells within the clinical volume receive adequate doses (Folkert *et al*., 2014).

The use of new radiation techniques, like IMRT has improved quality of life (QOL) and dose localizations, increasing local control and disease-free survival and at the same time a decrease in early and late effects of RT including bone fractures, oedema and joint stiffness (Hoefkens *et al*., 2016). Definitive radiotherapy for STS should be considered in clinical situations where no acceptable surgical option is available. Higher radiation doses yield superior tumor control and survival but, should be taken into account the complications that can occur in patients who receive doses over 68Gy (Kepka *et al*., 2005).

CI is also an appropriate tool in treatment plan analysis in 3D CRT and IMRT. The CI defined as following:

$$CI = \frac{\text{V95\%}}{Volume\ of\ PTV}$$

V95% is the volume of PTV covered by at least 95% of prescribed dose (Salimi *et al*., 2017).

The conformity index is a complementary tool that attributes a score to a treatment plan or that can compare several treatment plans for the same patient (Feuvret *et al*., 2006).

Dose conformality is important for large tumors such as sarcoma, providing adequate coverage of the periphery, and homogeneous coverage ensures that all tumor cells within the clinical volume receive the prescribed doses (Folkert *et al*., 2014).

The advantages of IMRT technique over 3D CRT and conventional techniques are reaching to the optimal dose distribution inside the tumor volume and decreasing the received dose by healthy tissues, these translate into improved outcomes and reduced toxicity (Feuvret *et al*., 2006).

In theory the advantages of IMRT over non-IMRT are well accepted but insufficient evidence is available to conclude for the clinical setting. The main argument to choose IMRT over non-IMRT is its capacity to reduce toxicity. Results regarding survival, tumor control or other indexes of treatment efficacy remain generally inconclusive. Comparative case series show no differences in disease control and survival, unless dose escalation was used. The use of RT biologically "sterilizes" microscopic extensions of tumor, this limiting the need for wide resection margins, and allowing sparing of critical organs or neurovascular bundles. Another possibly favorable aspect of preoperative RT is the potential reduction of the seeding of microscopic sarcomatous cells at the time of surgical resection in addition to tumor shrinkage itself, which will greatly enhance the ability of the surgeon to achieve negative margins (Hoefkens *et al*., 2016).

6. Conclusions

Pre- or postoperative Radiotherapy for STS of the extremity ensure excellent local control with acceptable treatment-related side effects but no statistically significant improvements in overall survival.

In the case presented above, we chose the IMRT irradiation technique even if in this case the CI was lower than the 3D-CRT techniques, in the desire to protect the OAR and another argument was the older age of the patient.

Also the percentage of volume receiving > 10Gy by the contralateral leg was lower by IMRT than 3D-CRT, reducing the risk of side effects or radiotherapy induced neoplasia.

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COMPARAȚIE DOZIMETRICĂ ÎNTRE TEHNICILE IMRT ȘI 3D-CRT ÎN RADIOTERAPIA POSTURGICALĂ A LIPOSARCOMULUI PLEOMORF DE COAPSĂ

(Rezumat)

Liposarcomul pleomorf reprezintă aproximativ 5% până la 15% din toate liposarcoamele și este mult mai agresiv decât alte subtipuri de liposarcom și este foarte rezistent la tratamentul convențional. Radioterapia a fost asociată cu o supraviețuire globală îmbunătățită comparativ cu intervenția chirurgicală singură. Prezentăm cazul unei paciente în vârstă de 74 de ani, diagnosticată cu liposarcom pleomorf, care, după o vindecarea completă după intervenția chirurgicală, a fost direcționată către

departamentul de radioterapie, unde a beneficiat de radioterapie externă postoperatorie în doză totală de 66Gy/33fr. Tehnica aleasă a fost radioterapia cu intensitate modulată, după ce a fost efectuată o comparație dozimetrică între tehnica cu intensitate modulată și tehnica tridimensională conformațională pe același volum tumoral. Utilizarea de noi tehnici de radiație, cum ar fi radioterapia cu intensitate modulată, a îmbunătățit calitatea vieții, a crescut controlul local și supraviețuirea fără progresia bolii și în același timp, o scădere a efectelor acute și tardive ale radioterapiei incluzând fracturile osoase, edemul și rigiditatea articulară.