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Three-dimensional treatment planning and treatment protocol in embryonal rhabdomyosarcoma and orthognathic surgery: A case report

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ABSTRACT

Rhabdomyosarcoma (RMS) is one of the most common soft tissue sarcomas encountered in paediatric patients. Embryonal rhabdomyosarcoma (ERMS), a variant of RMS, is observed in more than 70% of the cases and predominantly arises from head and neck region and genitourinary tract of children and young adults. Treatment is dependent on the size, location and extent of the tumor. This case report describes a 10 years old patient who received chemo- and radiotherapy. Three-dimensional (3D) conformal radiation therapy planning was carried out. The patient later suffered from asymmetric facial growth which was corrected with orthognathic surgery following 3D virtual surgical planning.

1. Introduction

Rhabdomyosarcoma (RMS) is a malignant tumor of neoplastic mesenchymal cells encompassing variable degrees of striated muscle cell differentiation [1]. RMS (Greek origin: rhabdo = rod, myo = muscle, sarkoma = fleshy growth) was first described by Weber (1854). Later on in 1946, Stout documented the distinct histopathological morphology of rhabdomyoblasts in this tumor [2]. RMS histological classification consists of four distinct subtypes, namely embryonal, alveolar, pleomorphic and undifferentiated form [3].

Embryonal rhabdomyosarcoma (ERMS) is considered to be the most common variant, accounting for more than 70% of RMS cases [4]. Based on its embryonal origin, it can occur at any anatomical location of the body irrespective of the skeletal muscle involvement. ERMS predominantly arises from head and neck region and genitourinary tract of children and young adults. Head and neck ERMS is most commonly observed in orbital and parameningeal areas, which include nasopharynx, nasal cavity, paranasal sinuses, pterygopalatine/infratemporal fossa and parapharyngeal space. In addition, non-parameningeal sites (oral cavity, oropharynx, larynx and parotid gland) can also be involved [5].

In RMS, three-dimensional conformal radiation therapy (3D CRT) planning is considered a valuable technique which specifically targets the tumor, thereby, avoiding the involvement of healthy tissue [6]. At the same instance, 3D planning in orthognathic surgery plays a vital role in improving the functional and aesthetic outcomes of a patient by overcoming the limitations associated with

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conventional two-dimensional planning [7]. We here describe a case with 3D treatment planning and treatment protocol in ERMS and orthognathic surgery.

2. Case report

This case report was in compliance with the World Medical Association Declaration of Helsinki on medical research. Ethical approval was obtained from the Ethical Review Board of the University Hospitals Leuven (Reference number: S58253) and informed consent was attained from the patient.

At the age of 10 years 10 months a female patient presented with ear pain and inability to eat for 2 weeks. Following evaluation from paediatric oncology clinic, ERMS was identified in the right parapharyngeal space with invasion of the right side of the oropharynx and nasopharynx with lung metastasis [Figure-1].

Chemotherapy was initiated according to Malginant Mesenchymal Tissue (MMT) 98 protocol (Ifosfamide, Vincristine and Adriamycin) [8]. Subsequently, radiation therapy treatment planning was performed in Eclipse software (version 8.6, Varian Medical Systems, Palo Alto, CA). Hereafter, a computed tomography (CT) scan (120 kVp, 3 mm slice thickness) of the patient, immobilized in treatment position using a 5-points thermoplastic mask, was acquired on a SOMATOM Sensation CT scanner (Siemens Healthineers, Erlangen, Germany) and rigidly co-registered with pre-chemo T2-weighted magnetic resonance images. Two clinical target volumes (CTV) were delineated, based on the gross tumor volumes (GTV) and accounting for potential microscopic spread and anatomical boundaries. CTV_1 included the pre-chemo GTV while CTV_2 included the post-chemo GTV. Organs at risk to be spared during treatment planning were delineated as well. To take into account positioning uncertainties during radiation therapy delivery, planning target volumes (PTV) were created by expanding the CTVs with a margin of 10 mm. The dose prescription was 50.4Gy to PTV_1 and 55.8 to PTV_2, both in fractions of 1.8 Gy using a sequential boost. Intensity-modulated radiation therapy planning was performed using a 5-field (gantry/couch angles: 325°/0°, 35°/0°, 150°/0°, 270°/350°; 20°/270°) sliding window technique on a Clinac 2100 C/D (Varian Medical Systems). Delivery of the plan was verified before the start of the treatment using portal dosimetry [9]. Thereafter, maintenance chemotherapy involving high risk arm RMS2005 was initiated, with daily oral administration of cyclophosphamide and D1, D8, D15 Vinorelbine IV (6 cycles for total period of 6 months) which led to the complete regression of the tumor [10].

Patient's skull and radiotherapy (RT) volume were segmented and registered in Amira software 6.5 for observing the 3D spread of radiation in maxillofacial area [Figure-2]. The patient developed postradiotherapy growth hormone (GH) deficiency and partial adrenocorticotropic hormone (ACTH) deficiency for which she received somatotropin (Nutropin Aq 1mg/day) and hydrocortisone (13mg/day). At the age of 14, patient developed central hypothyroidism for which she received elthyrone 50μg/day.

At the age of 17, patient was referred to oral and maxillofacial surgery clinic by her orthodontist for consultation regarding asymmetric face with mandible deviated towards the right side. Patient had a family history of breast cancer and burkitt's lymphoma. Dental history revealed agenesis of left mandibular permanent 2nd premolar, correction of posterior crossbite with hyrax palatal expansion device and orthodontic treatment for alignment of teeth. Systemic examination revealed normal cardiovascular, nervous, respiratory and abdominal functions.

Extra-oral findings revealed skeletal class II, convex profile, obtuse nasolabial angle and deviation of the chin towards the right side. Patient had posterior facial asymmetry with elongated mandible on the left side and a pronounced right cheek when compared to the left side [Figure-3a]. Maximum mouth opening of 36mm with no deviation on opening and closing of jaw. Facial height showed a ratio of 1:1:0.9. Intra-orally patient showed mandibular dental midline deviation of 1mm towards right. Skeletal midline deviation was observed 1mm and 4mm towards right side for maxilla and mandible respectively [Figure-3b]. The patient had an overjet of 3mm and overbite of 2mm.

Cone beam computed tomography (CBCT) showed normal corticalization and trabecular patterns of both jaws. Bone quantity and quality of both the jaws and periodontal areas was found to be normal. At the age of 18, extraction of left and right maxillary and

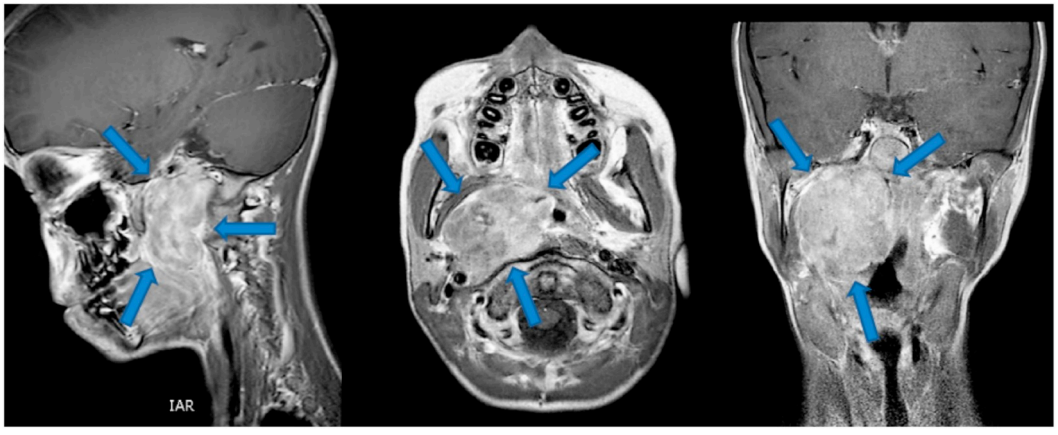

Fig. 1. Embryonal rhabdomyosarcoma spread to right parapharyngeal space, right side of the oropharynx and nasopharynx.

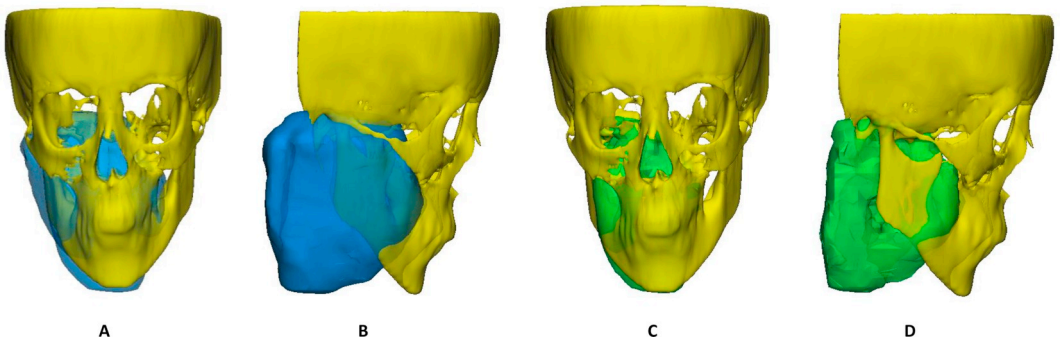

Fig. 2. 3D registration and visualization of planning target volume (PTV). **A, B,** Dose prescription of 50.4Gy to PTV_1. **C, D,** Dose prescription of 55.8Gy to PTV_2.

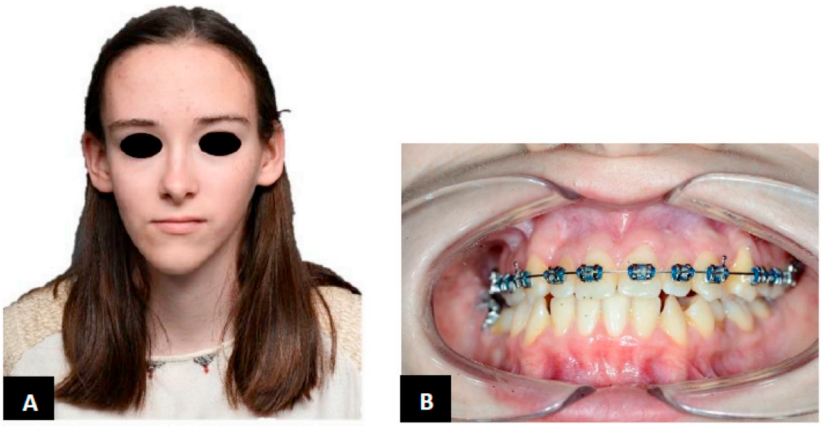

Fig. 3. Extra-oral and intra-oral findings. **A,** Frontal view of facial asymmetry. **B.** Intra-oral midline deviation.

mandibular third molars was carried out under general anaesthesia with normal but delayed healing.

The treatment plan for orthognathic surgery involved pre-surgical orthodontic levelling and alignment [Figure-4]. Patient was provided with hyperbaric oxygen (HBO) therapy before surgery. Based on the history of RT, pentoxyfilline and tocopherol were prescribed three months preoperatively to support bone healing and minocycline to prevent infection and bone resorption [11,12]. The mean associated radiation dose relative to the operative site was 44.3 Gy and the minimum dose was 10.9 Gy.

The virtual planning of the surgical procedure was defined by the surgeon with the application a surgical planning software (Synthes ProPlan CMF 3.0, Materialise, Leuven, Belgium). Surgical planning involved Le Fort 1 advancement of maxilla (4mm), Hunsuck/Epker modified bilateral sagittal split osteotomy (BSSO) rotation and transverse movement of mandible towards left side (2mm) and advancement genioplasty (4mm) [Figure-5]. Thereafter, intermediate and final splints were generated using the same software and printed using Objet Connex 350 (Stratasys) printer [13,14].

The surgery involved Le Fort 1 osteotomy fixed with two L-shaped long titanium miniplates plus mono-cortical screws on each side of the osteotomy. BSSO was fixed with two 4-hole straight miniplates with monocortical screws on the left side, two 4-hole straight miniplates and a single 6-hole double-Y shaped long miniplate on the right side. Autogenous bone graft harvested from anterior iliac crest was fixed onto the gap created by rotational movement of mandible during BSSO on the right using four separate monocortical

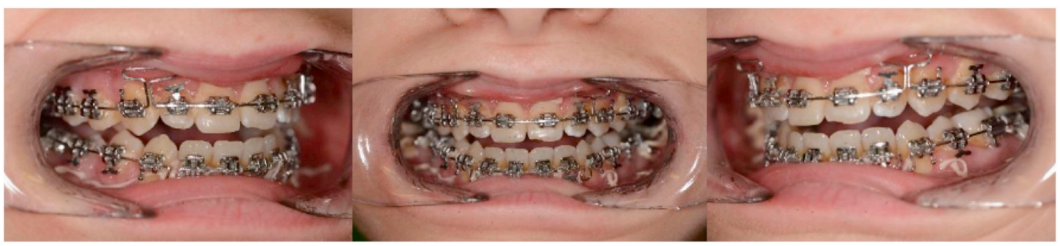

Fig. 4. Pre-surgical orthodontic levelling and alignment.

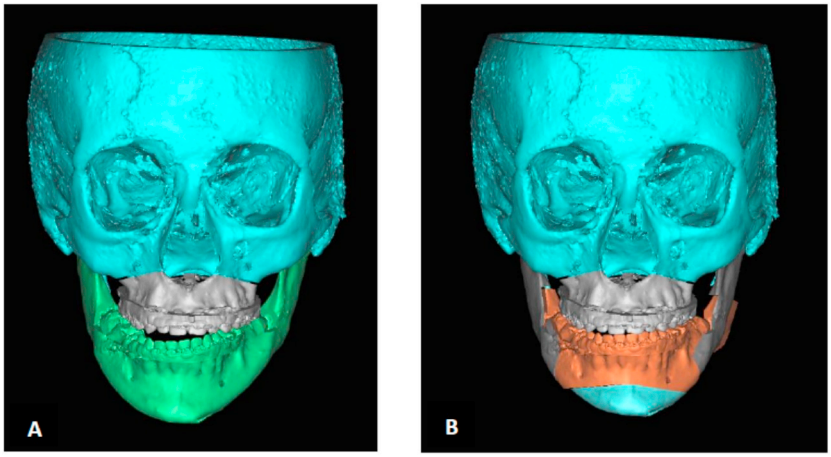

Fig. 5. A, 3-D Pre-operative virtual patient. **B,** Planned surgical movements involving Le Fort I, bilateral sagittal split osteotomy and advancement genioplasty.

screws. Low sliding genioplasty was carried out and fixed with a prebent 4-hole titanium plate (Stryker-Leibinger, Dallas, Texas).

Post-operative recovery was uneventful. Thirty sessions of post-operative HBO sessions were provided to the patient following surgery. Postoperative follow-up showed excellent functional and aesthetic results [Figure-6] with optimal soft tissue and bone healing. Patient is still undergoing further orthodontic treatment to stabilize the occlusion.

3. Discussion

Rhabdomyosarcoma is regarded as one of the most common paediatric soft tissue sarcoma affecting head and neck region in about 35% of cases [15]. Its clinical presentation is dependent on the location and extent of the tumor. Common clinical features include an enlarging mass with or without pain, limited mouth opening, facial palsy/paraesthesia and nasal discharge [16]. Distant metastasis may involve bone marrow, cerebrospinal/peritoneal fluid and lungs [17]. In our case study, the tumor did not spread to bone marrow, however it metastasized to the lungs which was managed by chemotherapy. The patients' overall treatment consisted of combined chemo- and RT, without any adenopathy or recurrence during follow-up.

The crossbite of the posterior teeth indicated towards retarded maxillary growth which was corrected by hyrax palatal expansion therapy, whereas lower jaw deviation pointed towards mandible growth retardation. In the present study, an asymmetric development of the jaw bones started after receiving RT and worsened over the next few years. RT commonly leads to hypovascularity and cytotoxicity of epiphyseal chondrocytes [18]. It effects craniofacial skeletal growth and maturation by damaging cartilaginous growth centres in condyles of mandible and sutural growth centres of maxilla [19]. At a radiation dose of 60–70Gy, paediatric patients are more prone to develop facial skeletal growth disturbances and associated malformations, however, depending on the age of patient, these disturbances can occur even at a lower dose [20,21]. Irradiation also has a deleterious effect on odontogenesis [17]. Tooth structure damage can be indirectly linked with radiation induced xerostomia. Dentition breakdown commonly initiates within 1st year following RT, thereafter, its affects become more detrimental with the passage of time. In patients receiving head and neck radiotherapy, minimal tooth damage can start at a radiation dose of below 30Gy, at a dose30-60Gy there is 2–3 times more likelihood of damage and 10 times increase in dental breakdown at a dose of above 60Gy [22]. Chemotherapy also has a direct effect on secretory functioning of GH and bone growth [18]. The combined radio- and chemotherapy factors might have influenced the growth retardation and jaw deviation in the patient. The 3D virtual planning of the RT showed the spread of the radiation which clinically effected the growth of the maxilla and mandible.

In paediatric patients, RT combined with chemotherapy are more prone to undergo structural and physiological changes. A surgical procedure in such areas are accompanied with grave complications which can include; osteoradionecrosis, infection, poor wound healing, growth retardation, mucositis, pain and difficult haemostasis [23,24]. To overcome these complications a proper management and surgical strategy should be designed in 3D from both oncological and orthognathic surgery perspective.

4. Conclusion

In future, we suggest registration of virtual 3D RT on a pre- orthognathic surgery CT/Cone-beam CT scan using cranial base as a reference and three dimensionally modification of osteotomy cuts away from the area involved in RT, if possible to reduce the possible associated complications.

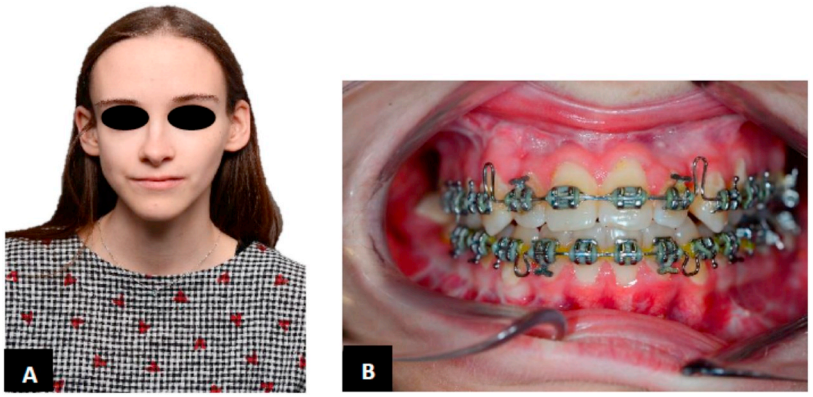

Fig. 6. A, 6 months postoperative frontal view. **B,** 6 months frontal view of post-operative occlusion.

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None.

Conflicts of interest

The authors report no conflict of interest.

Ethical approval

Ethical approval was obtained from the Ethics Review Board of the University Hospitals Leuven (S58253) and informed consent was attained from the patient.

References

[1] Joy T, Tupkari JV, Hanchate AV, Siwach P. Oral rhabdomyosarcoma in an adult male: a rare case report. J Oral Maxillofac Pathol 2018;22:285. https://doi.org/10.4103/jomfp.JOMFP_11_17.
[2] Stout AP. Rhabdomyosarcoma of the skeletal muscles. Ann Surg 1946;123:447–72.
[3] Iatrou I, Theologie-Lygidakis N, Schoinohoriti O, Tzermpos F, Vessala A-M. Rhabdomyosarcoma of the maxillofacial region in children and adolescents: report of 9 cases and literature review. J Cranio-Maxillofacial Surg 2017;45:831–8. https://doi.org/10.1016/j.jcms.2017.03.005.
[4] Arul ASKJ, Verma S, Arul ASSJ, Verma R. Oral rhabdomyosarcoma-embryonal subtype in an adult: a rarity. J Nat Sci Biol Med 2014;5:222–5. https://doi.org/10.4103/0976-9668.127347.
[5] Freling NJM, Merks JHM, Saeed P, Balm AJM, Bras J, Pieters BR, et al. Imaging findings in craniofacial childhood rhabdomyosarcoma. Pediatr Radiol 2010;40:1723–38. https://doi.org/10.1007/s00247-010-1787-3. quiz 1855.
[6] Lin C, Donaldson SS, Meza JL, Anderson JR, Lyden ER, Brown CK, et al. Effect of radiotherapy techniques (IMRT vs. 3D-CRT) on outcome in patients with intermediate-risk rhabdomyosarcoma enrolled in COG D9803 - a report from the children's oncology group. Int J Radiat Oncol Biol Phys 2012. https://doi.org/10.1016/j.ijrobp.2011.01.036.
[7] Chin S-J, Wilde F, Neuhaus M, Schramm A, Gellrich N-C, Rana M. Accuracy of virtual surgical planning of orthognathic surgery with aid of CAD/CAM fabricated surgical splint—a novel 3D analyzing algorithm. J Cranio-Maxillofacial Surg 2017;45:1962–70. https://doi.org/10.1016/J.JCMS.2017.07.016.
[8] McDowell HP, Foot ABM, Ellershaw C, Machin D, Giraud C, Bergeron C. Outcomes in paediatric metastatic rhabdomyosarcoma: results of the international society of paediatric oncology (SIOP) study MMT-98. Eur J Cancer 2010;46:1588–95. https://doi.org/10.1016/J.EJCA.2010.02.051.
[9] Van Esch A, Depuydt T, Huyskens DP. The use of an aSi-based EPID for routine absolute dosimetric pre-treatment verification of dynamic IMRT fields. Radiother Oncol 2004;71:223–34. https://doi.org/10.1016/J.RADONC.2004.02.018.
[10] Bisogno G, Bergeron C, Jenney M. European paediatric soft tissue sarcoma study group RMS 2005: a protocol for non-metastatic rhabdomyosarcoma 2005. 2008., Version 1.2.
[11] Garrido-Mesa N, Zarzuelo A, Gálvez J. Minocycline: far beyond an antibiotic. Br J Pharmacol 2013;169:337–52. https://doi.org/10.1111/bph.12139.
[12] Owosho AA, Estilo CL, Huryn JM, Yom SK. Pentoxifylline and tocopherol in the management of cancer patients with medication-related osteonecrosis of the jaw: an observational retrospective study of initial case series. Oral Surg Oral Med Oral Pathol Oral Radiol 2016;122:455–9. https://doi.org/10.1016/j.oooo.2016.06.019.
[13] Shaheen E, Sun Y, Jacobs R, Politis C. Three-dimensional printed final occlusal splint for orthognathic surgery: design and validation. Int J Oral Maxillofac Surg 2017;46:67–71. https://doi.org/10.1016/j.ijom.2016.10.002.
[14] Shaheen E, Coopman R, Jacobs R, Politis C. Optimized 3D virtually planned intermediate splints for bimaxillary orthognathic surgery: a clinical validation study in 20 patients. J Cranio-Maxillofacial Surg 2018;46:1441–7. https://doi.org/10.1016/j.jcms.2018.05.050.
[15] Radzikowska J, Kukwa W, Kukwa A, Czarnecka AM, Kawecki M, Lian F, et al. Management of pediatric head and neck rhabdomyosarcoma: a case-series of 36 patients. Oncol Lett 2016;12:3555–62. https://doi.org/10.3892/ol.2016.5072.
[16] Shrutha SP, Vinit GB. Rhabdomyosarcoma in a pediatric patient: a rare case report. Contemp Clin Dent 2015;6:113–5. https://doi.org/10.4103/0976-237X.149305.
[17] Zhou D-N, Yang Q-Q, Li Z-L, Pan Z-Y, Deng Y-F. Head and neck rhabdomyosarcoma: follow-up results of four cases and review of the literature. Int J Clin Exp Pathol 2015;8:4277–83.
[18] Dahllöf G, Huggare J. Orthodontic considerations in the pediatric cancer patient: a review. Semin Orthod 2004;10:266–76. https://doi.org/10.1053/J.SODO.2004.09.007.
[19] Otmani N. Oral and maxillofacial side effects of radiation therapy on children. J Can Dent Assoc 2007;73:257–61.

[20] Krasin MJ, Constine LS, Friedman DL, Marks LB. Radiation-Related treatment effects across the age spectrum: differences and similarities or what the old and young can learn from each other. Semin Radiat Oncol 2010;20:21–9. https://doi.org/10.1016/j.semradonc.2009.09.001.
[21] Deshpande TS, Dhokar A. Oral complications of non-surgical cancer therapies: a review. Int J Prev Clin Dent Res 2015;2:52–7.
[22] Walker MP, Wichman B, Cheng A-L, Coster J, Williams KB. Impact of radiotherapy dose on dentition breakdown in head and neck cancer patients. Pract Radiat Oncol 2011;1:142–8. https://doi.org/10.1016/j.prro.2011.03.003.
[23] ROBINSON DW. The hazards of surgery in irradiated tissue. Arch Surg 1955;71:410. https://doi.org/10.1001/archsurg.1955.01270150104012.
[24] Karr RA, Kramer DC, Toth BB. Dental implants and chemotherapy complications. J Prosthet Dent 1992;67:683–7. https://doi.org/10.1016/0022-3913(92)90171-6.