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Radiological changes with magnetic resonance imaging and computed tomography after irradiating minipig mandibles: The role of T2-SPIR mixed signal intensities in the detection of osteoradionecrosis

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ABSTRACT

Purpose: Radiotherapy in the head and neck can induce several radiologically detectable changes in bone, osteoradionecrosis (ORN) among them. The purpose is to investigate radiological changes in mandibular bone after irradiation with various doses with and without surgery and to determine imaging characteristics of radiotherapy and ORN in an animal model.
Materials and methods: Sixteen Göttingen minipigs were divided into groups and were irradiated with two fractions with equivalent doses of 0, 25, 50 and 70 Gray. Thirteen weeks after irradiation, left mandibular teeth were removed and dental implants were placed. CT-scans and MR-imaging were made before irradiation and twenty-six weeks after. Alterations in the bony structures were recorded on CT-scan and MR-imaging and scored by two head-neck radiologists.
Results: Increased signal changes on MR-imaging were associated with higher radiation doses. Two animals developed ORN clinically. Radiologically mixed signal intensities on T2-SPIR were seen. On CT-scans cortical destruction was found in three animals. Based on imaging, three animals were diagnosed with ORN.
Conclusion: Irradiation of minipig mandibles with various doses induced damages of the mandibular bone. Imaging with CT-scan and MR-imaging showed signal and structural changes that can be interpreted as prolonged and insufficient repair of radiation induced bone damages.

1. Introduction

Treatment of head and neck malignancies frequently includes radiotherapy (RT), which has been demonstrated to have beneficial effects on locoregional recurrence and survival (Peters et al., 1993; Bourhis et al., 2006). However, despite improved radiotherapeutic techniques, inevitable irradiation effects on the surrounding healthy tissue are still a concern in terms of complications (Lee and Moon, 2011; Thariat et al., 2011).

Osteoradionecrosis (ORN) occurs especially in the mandible and is considered a serious complication of RT. ORN can be triggered by surgery or can occur spontaneously. It can arise at any moment after RT, even after several years. If conservative treatment of ORN fails, radical resection and micro-vascular reconstruction is indicated, requiring a major surgical intervention (Jereczek-Fossa and Orecchia, 2002; Jacobson et al., 2010).

The most commonly used definition of ORN is based on clinical presentation and observation: “irradiated bone becomes devitalized and is no longer covered by skin or mucosa without healing for 3 months, without recurrence of tumor” (Lyons and Ghazali, 2008). The reported incidence of ORN in literature ranges between 2% and 22% for the mandible (Teng and Futran, 2005). Several factors that can increase the risk of developing ORN have

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been identified, and include, for instance, age, sex, general health, smoking, and dose and volume of irradiation (Teng and Futran, 2005; Lyons and Ghazali, 2008). Marx and Johnson discovered a double peak in occurrence at 1 year and approximately 4 years after irradiation (Marx and Johnson, 1987). Several classifications for ORN exist, the most practical being the Notani classification: Class I ORN is confined to dentoalveolar bone; class II ORN is limited to dentoalveolar bone or mandible above the inferior dental canal, or both; and class III ORN is characterized by involvement of the mandible below the inferior dental canal, pathological fracture, or skin fistula (Notani et al., 2003).

The susceptibility of the mandible to developing ORN is mainly the result of RT-induced fibrosis of the bone marrow that causes obliteration of the inferior alveolar artery. As the facial artery is incapable to supply sufficient collateral blood supply, ORN occurs (Zhuang et al., 2011).

1.1. Imaging findings

To the best of our knowledge, only a few studies on magnetic resonance imaging (MRI) changes in the mandible after irradiation exist (Bachmann et al., 1996; Store et al., 2000; Deshpande et al., 2015). Known MRI changes in bone marrow in vertebrae and the femur head after irradiation consist of decreased signal intensity on T1-weighted (T1) and T2-weighted (T2) images may show mixed signal intensity corresponding to areas of bone marrow edema pattern (BMEP) and fibrosis after 6 weeks and onwards. With chronicity, focal areas of fat may be deposited, which, on T1 images, will appear as areas of increased signal intensity. Fibrosis and areas of sclerosis are characterized by hypointense signal on both T1 and T2 images (Stevens et al., 1990; Tartaglino et al., 1994).

Bachman et al. described MRI findings of the mandible after RT. They stated that tooth extraction in or resection of irradiated mandibular bone causes localized oedema of the alveoli or resection margins. However, periodontal disease in irradiated bone causes only minimal BMEP or no signal abnormalities at all on MRI (Bachmann et al., 1996). Furthermore, they conclude that MRI allows detection of pathologic changes of mandibular bone marrow in ORN. The inflammatory process is diffusely disseminated in the mandible, often not respecting the cortical boundaries and invading paraossal tissue. Signal characteristics of BMEP on MRI consist of reduced signal intensity on T1 images and increased signal intensity on T2 images (Bachmann et al., 1996). Store et al. found that several years after RT, no difference in signal intensity between irradiated and non-irradiated, normal mandibular bone was visible anymore (Store et al., 2000).

Typical computed tomography (CT) findings of ORN in the literature consist of cortical disruption with disorganization and loss of trabeculation of the spongiosa of the mandible (Hermans et al., 1996). Cortical bone fragmentation is present in most cases (Hermans et al., 1996). In more severe cases, pathologic fracture can occur (Fujita et al., 1991). Cortical thickening may be present (Tartaglino et al., 1994).

These abnormalities are predominantly seen in the body of the mandible (premolar and molar region). In some cases, even extension into the mandibular angle or retromolar triangle can be found (Chong et al., 2000).

1.2. Purpose of this study

Since there is only limited literature available on RT-induced structural changes in the mandible, the aim of our study was to describe imaging findings in mandibular bone after various doses of irradiation, with and without surgery, in order to identify typical imaging characteristics of post-irradiation changes and ORN.

2. Materials and methods

2.1. Research design

In this animal study, 16 healthy adult 18 month-old female Göttingen minipigs were used (weight 35–45 kg). The study was performed in accordance with the Dutch and European Community guidelines for the protection of (laboratory) animals and was partly described in our earlier publications (Poort et al., 2014, 2015). Permission was obtained from the local Animal Ethical Committee (DEC 2011-127).

2.2. Procedures

After initial baseline imaging, consisting of CT and MRI, RT as described below took place. Then, 13 weeks later, surgery was performed. At 26 weeks after RT, imaging was repeated, using MRI protocols identical with the baseline scans.

2.3. Imaging

For irradiation planning purposes, a CT scan (Siemens Sensation Open, 120 kV, 270 mAs, CDTI/vol 29,32 mGy, 0.6 mm slices, FOV 500 mm, matrix 512 × 512, Siemens, Erlangen, Germany) was performed under general anaesthesia using an individualised thermoplastic immobilisation mask for optimal fixation of the animal, made immediately before scanning. The CT scan was directly followed by a 1.5-T MRI scan (1.5 T Intera, Philips Healthcare, Best, the Netherlands), still under anaesthesia but without the immobilisation mask. Six months after irradiation, CT (Siemens Somatom Definition Flash, Dual Scource, Dual Energy tube A Sn 140 kV, 225 mAs, tube B 80 kV–450 mAs, CDTI vol 38.15 mGy, 0.6 mm slices, FOV 300 mm, matrix 512 × 512, Siemens Erlangen, Germany) and MRI were repeated under general anaesthesia. Immediately after imaging, the animals were sacrificed. The MRI protocol consisted of coronal T1, T2 and T2-SPIR, transverse STIR images, and coronal post-gadolinium T1 images of the mandible using a head-coil (T1 sequence, TR/TE = 530/11 ms, T2 sequence, TR/TE = 3600/80 ms, T2-SPIR, TR/TE = 3700/80 ms, STIR, TR/TE = 3900/15 ms, T1 sequence after gadolinium (Gadobutrol 1.0 mmol/ml; 7.5 ml i.v., 0.2 mmol/kg), TR/TE 470/15 ms, FOV 220–240 mm and slice thickness 3.0 mm).

2.4. Irradiation

Four animals each were assigned to one of the four groups receiving an equivalent dose (EQD) of 0, 25, 50 or 70 Gray (Gy), respectively. Irradiation took place under general anaesthesia, 1 week after imaging. For optimal positioning, the animals were immobilised using an individualized thermoplastic mask for the treatment planning CT as well as the radiation fractions. For irradiation, a 6-MV linear accelerator (Linac Siemens, Erlangen, Germany) with two opposing lateral beams was used. The entire body of the mandible was irradiated in two fractions with an equivalent dose of 0, 25, 50 or 70 Gy (two fractions of 0, 6.5, 9.7 and 11.8 Gy). In order to calculate the equivalent dose, an alpha/beta ratio of 3 was used for late responding tissues using the linear quadratic formula (Fowler, 2010). The second fraction was given 48 h after the first fraction.

2.5. Surgical intervention

Thirteen weeks after irradiation, surgery was performed under general anaesthesia.