Krisztina Emeriewen MD¹, Mandeep S. Sagoo BSc, MB, PhD, MRCOphth, FRCSEd^{1,2,3}, Michael Simpson BDS, MBBS, MRCS, FFDRCS⁴, Judith Kingston BSc, FRCP, FRCPCH ⁵, George M Saleh BSc, FRCS, FRCOphth^{1,3,6}

Moorfields Eye Hospital NHS Foundation Trust, London, UK, EC1V 2PD
Retinoblastoma Unit, Royal London Hospital, London, E1 1BB
UCL Institute of Ophthalmology, London, EC1
Bedford Hospital NHS Foundation Trust, Bedford, UK, MK42 9DJ
Great Ormond Street Hospital, NHS Trust, London, UK, WC1N 3JH
The National Institute for Health Research Biomedical Research Centre at Moorfields Eye Hospital and the UCL Institute of Ophthalmology, London, UK

Corresponding author:

Krisztina Emeriewen Moorfields Eye Hospital NHS Foundation Trust Kempston road, Bedford, UK, MK429DJ Email: <u>krisztinaemeriewen@yahoo.com</u> Tel: 07462064070

RUNNING TITLE: Very late onset orbital sarcoma and breast carcinoma following retinoblastoma treatment with Radon seed brachytherapy.

KEYWORD: Retinoblastoma, Breast cancer, Radiation, Osteosarcoma, Radon

Dear Editor,

We report a case of an 87-year-old white female presenting with a history of a non-tender right orbital swelling. She had subtotal exenteration for unilateral Retinoblastoma (RB) at age three followed by Radon seed implantation removed 27-years later but received no chemotherapy.

Although radon seeds were encapsulated in gold tubes allowing gamma-ray passage for tumour destruction (whilst blocking alpha and beta particles that can risk tissue necrosis), the decay product (²¹⁰Pb) continued to emit radiation for a longer period of time associated with increasing cancer risk, hence the use was discontinued after the 1960s.¹

At 82-years-old she was diagnosed with grade-2 invasive ductal carcinoma of the left breast (oestrogen receptor-positive subtype). The RB pathway has been associated with a less aggressive course in this subtype and nonheritable RB survivors are more prone to radiation related breast cancer.^{2,3} No genetic testing was available to confirm a germline RB1 or mosaic mutation. This case highlights the potential adverse consequence in the radiation field with multiple basal cell carcinomas developing over a 20-year period post radiation and she also fits the criteria of post irradiation sarcoma described by Cahan et al in 1985, which is most commonly encountered 15 years post radiation (reported up to 50 years) unlike the present case, where the sarcoma occurred 84 years later.^{4,5,6}

Though there has been a paradigm shift in RB management from radiation to chemotherapy, a careful history of previous, now superseded treatments in late survivors is mandatory, as is awareness of their very late effects.

References

 Mc Laughlin J. An historical overview of radon and its progeny: applications and health effects. Radiat Prot Dosimetry. 2012 Nov; 152(1-3): 2-8

- Agnieszka K Witkiewicz, Erik S Knudsen. Retinoblastoma tumor suppressor pathway in breast cancer: prognosis, precision medicine, and therapeutic interventions. Breast Cancer Res. 2014 May 7; 16(3): 207
- Little MP, Schaeffer ML, Reulen RC, Abramson DH, Stovall M, Weathers R, de Vathaire F, Diallo I, Seddon JM, Hawkins MM, Tucker MA, Kleinerman RA. Breast cancer risk after radiotherapy for heritable and non-heritable retinoblastoma: a US-UK study. Br J Cancer. 2014 May 13; 110 (10): 2623-32.
- Des Guetz G, Chapelier A, Mosseri V, Dorval T, Asselain B, Pouillart P. Postirradiation sarcoma: clinicopathologic features and role of chemotherapy in the treatment strategy. Sarcoma. 2009; 2009: 764379
- 5. Yonemoto T, Hosono A, Iwata S, Kamoda H, Hagiwara Y, Fujiwara T, Kawai A, Ishii T. The prognosis of osteosarcoma occurring as second malignancy of childhood cancers may be favorable: experience of two cancer centers in Japan. Int J Clin Oncol. 2015 Jun; 20(3): 613-6
- Lee JA, Choi SY, Kang HJ, Lee JW, Kim H, Kim JH, Sung KW, Shin HY, Ahn HS, Park KD. Treatment outcome of osteosarcoma after bilateral retinoblastoma: a retrospective study of eight cases. Br J Ophthalmol. 2014 Oct; 98(10): 1355-9.

