“Real World” Experience of using Stereotactic Radiotherapy to treat neovascular AMD in a cohort of patients at Manchester Royal Eye Hospital

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Introduction

Capacity for intravitreal injection (IVI) treatment clinics is a serious concern and the impact of undergoing repeated visits for frequent treatment is an ongoing problem to patients and carers. Adjunctive treatment or longer-acting drugs are required to help ease these burdens for patients and hospital clinics alike. Stereotactic therapy is one such option, providing a reduction in the number of injections over time.

A stereotactic radiotherapy (SRT) device (IRay; Carl Zeiss Meditec) designed specifically to treat neovascular age-related macular degeneration (nAMD) delivers low-voltage x-rays non-invasively through the inferior pars plana to focus on the macula, targeting the DNA of rapidly dividing cells[1].

The INTREPID clinical trial showed that SRT significantly reduced the frequency of anti-VEGF injections over one and two years[2,3], with the best responders receiving 45% less anti-VEGF injections compared to the sham group after two years.

Objective:

To determine the clinical outcomes in a cohort of patients with nAMD and meeting the best responder’s criteria as per the INTREPID study[4], receiving a combination therapy of stereotactic radiotherapy (SRT) with intravitreal anti-VEGF injections (IVI).

Method:

A retrospective analysis of 74 patients with nAMD, who had received IVI and SRT at Manchester Royal Eye Hospital, between March 2018 and September 2019 was performed. This cohort of patients had at least 12 months of IVI treatment prior to SRT. All patients with a minimum of 12 months of follow up data following SRT are presented. For a subset of these 74 patients, data is also being presented for 24 and 36 months follow up (n=48 and n=22 respectively). Number of IVIs, Visual Acuity (VA) and Central Retinal Thickness (CRT) were evaluated at 12, 24 and 36 months after patients received SRT and compared to the same time interval prior to SRT.

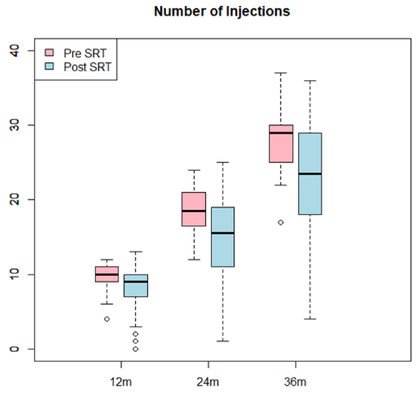


***Figure 1**. A box and whisker plot of the numbers of injections pre and post SRT at of 12, 24 and 36 months.*

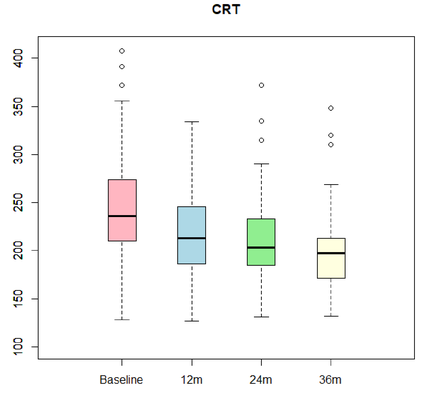


***Figure 2**. A box and whisker plot of CRT at baseline and post SRT where CRT is measured in µm*

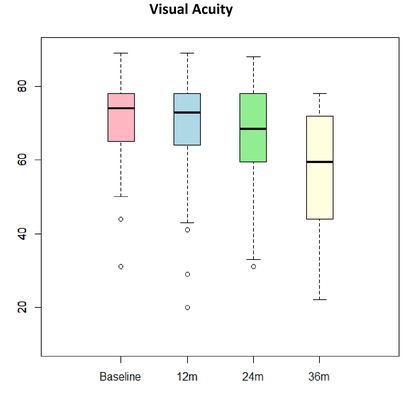


***Figure 3.** A box and whisker plot of Visual Acuity at baseline and post SRT, where VA is measured in ETDRS letters*

OCT- Angiography (OCTA) on the day of SRT (A) and 6 months post SRT (B)

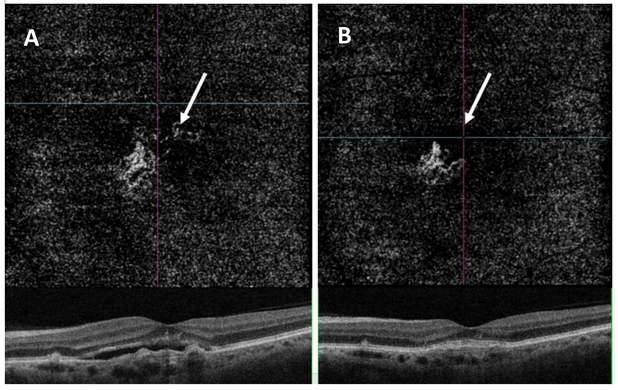


Figure 4. OCTA and OCT imaging of a patient with nAMD before and after SRT. The white arrows show the reduction in size of the choroidal neovascular membrane. This patient had received 26 IV ranibizumab injections over four and a half years. His treatment was switched to aflibercept and he underwent a further nine monthly injections at which point there was still persistent disease activity. After switching back to ranibizumab, this patient underwent SRT. The white arrows show a reduced choroidal neovascular membrane and an OCT image with no subretinal fluid. This patient did not require any further injections until a reactivation of disease two years later.

OCT- Angiography (OCTA) on the day of SRT (C) and 9 months post SRT (D)

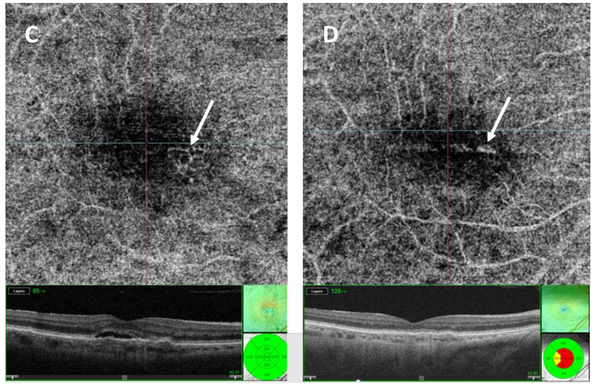


Figure 5. OCTA and OCT imaging of a patient with nAMD before and after SRT. The white arrows show the position of the choroidal neovascular membrane. This patient had received 4 to 6 weekly injections of ranibizumab over three years. Following SRT, the patient was treated on a treat and extend basis and was able to reduce her visits to every 12 weeks with stable visual acuity. The OCTA shown was taken 9 months after the SRT and at the point of a twelve week extension visit.

Results

Overall there was a significant reduction in number of injections post SRT. Twelve months following SRT, the median number of IVI were reduced by 1 ($p < 0.05$). The reduction in median number of IVI was significantly reduced by 3 and 6 injections at 24- and 36-month follow-up respectively ($p < 0.05$) (***figure 1***).

The CRT was significantly reduced post SRT compared to the baseline values at all time periods (***figure 2***).

There was no statistically significant difference in VA at 12-months follow-up compared to baseline. The VA, however, significantly decreased at 24- and 36-months follow-up ($p<0.05$) (***figure 3***).

Figures 4 and **5** show examples of patients with resolution of active features of choroidal neovascular membrane on OCT and OCTA after SRT treatment.

Conclusion:

A therapy combining SRT with IVI has shown an overall reduction in number of injections required in nAMD patients in the first 12 months following SRT compared to IVI treatment alone. The number of IVI required continued to reduce at the 24 and 36-months follow-up.

SRT as an adjunctive treatment option in addition to IVI may be beneficial in reducing the treatment burden for patients with nAMD. This treatment option may also be suitable for patients who are very anxious and not keen for repeated or frequent injections. Whilst this treatment is currently not available, our real world data contributes to the evidence.



***Figure 6**. Stereotactic radiotherapy (SRT) device (IRay; Carl Zeiss Meditec)*

References:

1. Darius M Moshfeghi, Peter K Kaiser, Michael Gertner. Stereotactic low-voltage x-ray irradiation for age-related macular degeneration. Br J Ophthalmol. 2011 Feb;95(2):185-8.
2. Timothy L. Jackson, Usha Chakravarthy, Peter K. Kaiser, Jason S. Slakter, Ernest Jan, Francesco Bandello, Denis O’Shaughnessy, Michael E. Gertner, Linda Danielson, Darius M. Moshfeghi on behalf of the INTREPID Study Group. Stereotactic Radiotherapy for Neovascular Age-related Macular Degeneration 52-Week Safety and Efficacy Results of the INTREPID Study. Ophthalmology 2013;120:1893–1900.
3. Timothy L. Jackson, Usha Chakravarthy, Jason S. Slakter, Alyson Muldrew, E. Mark Shusterman, Denis O’Shaughnessy, Mark Arnoldussen, Michael E. Gertner, Linda Danielson, Darius M. Moshfeghi, on behalf of the INTREPID Study Group. Stereotactic Radiotherapy for Neovascular Age-Related Macular Degeneration Year 2 Results of the INTREPID Study. Ophthalmology 2015;122:138-145.
4. Timothy L. Jackson, E. Mark Shusterman, Mark Arnoldussen, Erik Chell, Kun Wang, Darius M. Moshfeghi, on behalf of the INTREPID Study Group. Stereotactic Radiotherapy for Neovascular Age-Related Macular Degeneration (INTREPID) Influence of Baseline Characteristics on Clinical Response. RETINA 35:194–204, 2015.