Image-Guided Rhenium-186 NanoLiposome (^{186}RNL) Brachytherapy In The Treatment Of Recurrent Glioblastoma: Technique, Image Analysis, Dosimetry, And Monitoring

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INTRODUCTION

^{186}Rhenium-lipid nanoparticles (^{186}Re-nanoliposomes, ^{186}RNL) has been introduced in the focused brachytherapy of cancers via image-guided infusion to the tumor interstitial space; firstly, in the treatment of recurrent glioblastoma of brain (GBM). Rhenium-186 (^{186}Re) is a radionuclide (half-life: 89.24 hours) emitting therapeutic beta-radiation particles (path range: 1.8 mm). One of every 10 emissions is associated with a 137 KeV gamma ray allowing imaging of *in vivo* drug distribution, retention, and for radiation absorbed dose distribution calculation and therapy evaluation. Herein, we report our Phase I clinical Trial study with the focus on technique used, image analysis, radiation dosimetry, and therapy monitoring.

AIM

While external beam radiation therapy (EBRT) remains a central component of the management of gliomas, it is limited by tolerance of the surrounding normal brain tissue. We hypothesized that Rhenium-186 NanoLiposome (^{186}RNL) focused brachytherapy will permit the selective delivery of high specific activity beta-emitting radiation with excellent retention in the tumor and that the emitted gamma rays will permit real time image-guided delivery and monitoring. Herein, we report the technique used, imaging of the nanoliposome distribution and retention, image analysis, radiation dosimetry, and therapy monitoring.

METHOD

A Phase 1 clinical trial of ^{186}RNL administered by convection enhanced delivery (CED) through a Brainlab flexible subacute catheter to treat recurrent glioblastoma was conducted. BrainLab iPlan Flow Software and Varioguide system were used for treatment planning and catheter placement. The retention and distribution of ^{186}RNL within the tumor and whole body were obtained by planar and SPECT/CT imaging from mid-infusion to 8 days following radiation source administration. Locoregional and whole body drug retention were analyzed from whole body planar images. SPECT/CT and follow-up MR images were co-registered to planning MR images for 3D drug distribution and therapy evaluation. Radiation absorbed doses to local volumes and whole body organs were calculated.

Using MIM MRT quantitative SPECT image reconstruction and 3D dose calculation, 3D radiation absorbed dose distribution of ^{186}RNL therapy in 8 days has been calculated, and evaluated with tumor therapy response.

RESULTS

^{186}RNL delivered by CED to patients with recurrent glioblastoma results in predictable distribution and stable retention of nanoparticle radiation source in the targeted tissues, providing days of sustained, localized radiation treatment to the tumor (*Fig. 1*).

The use of up to four catheters effectively enhances locoregional drug distribution and tumor volume coverage. The mean locoregional retention in the brain volume at the end of infusion was 85.9% ± 17.1% ID (n = 18) and at 8 days post-infusion was 46.6% ± 16.7% ID (n = 17). Following dose escalation, the mean radiation absorbed dose in the two most recent cohorts to the tumor volume was 354.7 ± 144.0 Gy, to the whole brain was 1.32 ± 1.06 Gy, and to the whole body was 0.16 ± 0.04 Gy (n = 6).

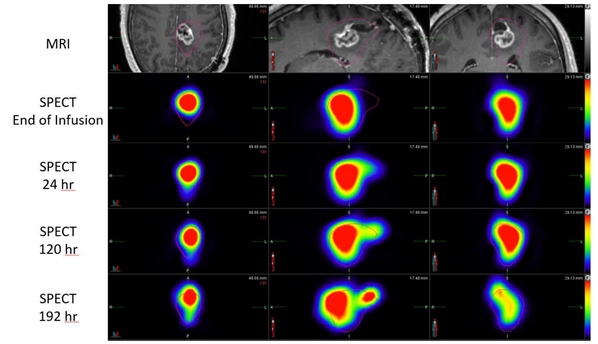


Fig. 1. Distribution and retention of ^{186}RNL radiation source in 8 days after infusion. ^{186}RNL radiation source had sustained retention and stable locoregional distribution at tumor to be treated in the brain, which provided the continuous radiation therapy effect in over 8 days.

Fig. 2 shows a 3D dose distribution and DVH in the tumor and nearby tissue. With the treatment technique, the radiation absorbed dose in the treated volume were a few hundred Gy or higher, while radiation absorbed dose beyond the distribution volume of radiation source dropped rapidly to a minimal level (White arrow in *Fig. 2.A* shows the 5-Gy isodose line). For the comparison, *Fig. 2* also illustrated an example of SBRT cases with the isodose distribution in the tumor and surrounding normal tissue. In the SBRT case with 30-Gy prescribed dose to PTV, the white arrow in *Fig. 2.C* shows the 5-Gy isodose line as a comparison.

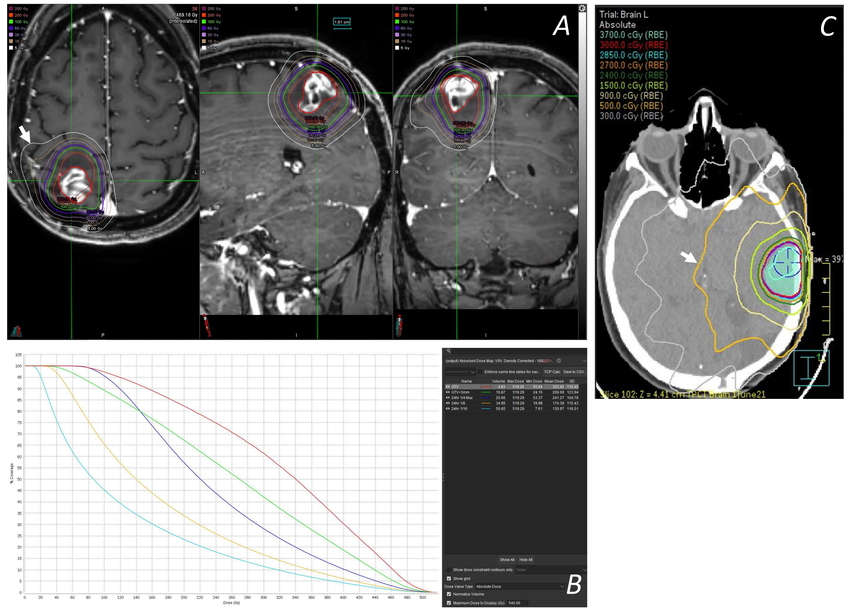


Fig. 2. 3D dose distribution of ^{186}RNL brachytherapy (*A*) and DVH (*B*). In the Case shown, the maximum dose in the treated volume was > 500 Gy, the mean dose to GTV was 323 Gy, and minimum dose to GTV was 55.6 Gy in 8 days. An important feature of the treatment technique is the highly focused treatment to the volume with radiation source delivery. The 3D dose distribution has shown a very sharp dose gradient; the 5 Gy isodose line has been shown (*white arrow*). For the comparison, *Fig. 2.C* illustrates the isodose distribution of an SBRT case. This focused brachytherapy treatment allows for a high radiation dose treatment for tumor eradication, while with low toxicities to un-involved tissue.

CONCLUSIONS

- ^{186}RNL brachytherapy provides a high radiation absorbed dose to the tumor with minimal brain and whole body radiation exposure.
- The therapy from this technique also provides a sustained radiation to the target from high to low radiation dose rates for over 8 days, which can be beneficial in radiobiology on tumor control.
- Comparing with sealed source brachytherapy, it can be advantageous in minimal invasiveness, planning, and convenience of delivery.
- The image monitoring capability can provide a predictive tool to evaluate therapy delivery and treatment effectiveness.
- The development of 3D dose distribution calculation makes it convenient for dose and therapy effect evaluation, and for the application of additional therapy for better tumor control.

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