# Multicentre study of frameless stereotactic radiosurgery for breast cancer brain metastases

Eric K Oermann BS; Marie-Adele S Kress MD; David Morris; Jing Wu MD, PhD; Riane B Hoffman BA; Sean P. Collins MD, PhD; Huma Chaudry BS; Brian T. Collins MD; Matthew G. Ewend MD

Departments of Neurosurgery and Radiation Oncology, The University of North Carolina at Chapel Hill, Chapel Hill, NC

Department of Radiation Medicine, Georgetown University, Washington, DC

## Learning Objectives

By the conclusion of this session, participants should be able to: 1) Describe the outcomes of patients with breast cancer brain metastastes treated with frameless radiosurgery, 2) Discuss the use of neurosurgical interventions that can facilitate single fraction radiosurgery and superior outcomes.

## Introduction

Due to excellent systemic treatment options and the potential for long survival, the development of brain metastases poses a clinical challenge when treating patients with primary breast cancer. This study reports on the outcomes of a multicenter study using frameless stereotactic radiosurgery alone or with surgical resection.

## Methods

Patients from Georgetown University Hospital and the University of North Carolina at Chapel Hill were retrospectively gathered into a comprehensive database. All patients had newly diagnosed intracranial metastases in the context of a primary diagnosis of breast carcinoma. Adjuvant and salvage WBRT were used at the discretion of the treating radiation oncologist. Pre-treatment variables were analyzed for correlation with overall survival, local control, and distal control using non-parametric statistical testing and Cox hazard regression.

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**Table 1**

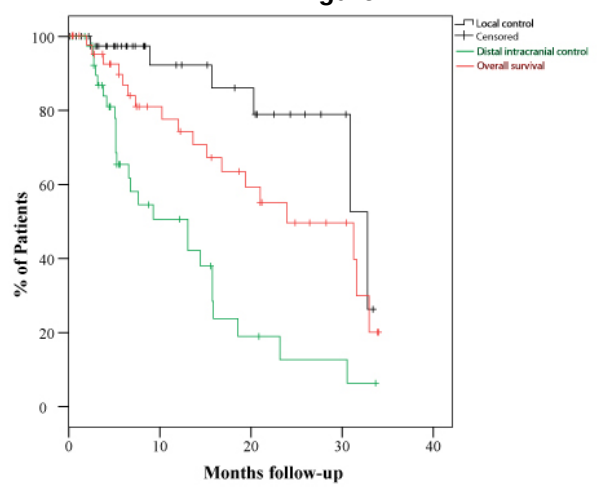
| Hormone Group | Average Survival (months) | | | |
|---|---|---|---|---|
| | Estimate | Std. Error | 95% Confidence Interval | |
| | | | Lower Bound | Upper Bound |
| HR-/HER2- | 13.6 | 3.7 | 6.3 | 20.8 |
| HR+/HER2- | 18.5 | 3.9 | 10.8 | 26.2 |
| HR-/HER2+ | 23.7 | 4.1 | 15.6 | 31.8 |
| HR+/HER2+ | 24.1 | 3.2 | 17.9 | 30.2 |
| Overall | 21.8 | 2.1 | 17.7 | 26.0 |

Survival outcomes stratified by molecular subtype.

## Results and Discussion

43 patients with favorable performance status and mild neurological symptoms were included in the study. The distribution of breast cancer molecular subtypes was relatively equal with a slight predominance of HER2 positive tumors. 75% of patients had 2 or fewer intracranial metastases with an average diameter of 1.88 cm (SD, 1.02 cm) with the majority located in the frontal and parietal lobes. The actuarial overall survival was 21.8 months (95% C.I. 17.7-26 months). The average actuarial distal intracranial control was 12.7 months (95% C.I. 5.5 – 19.9 months), with 41.9% of the patients ultimately experience distal brain recurrences (Figure 1). Distal intracranial control was correlated with HER2 positivity (p=0.047) and pre-treatment WBRT (p= 0.014) on multivariate regression analysis. The average actuarial local control was 28.5 months (95% C.I. 24.9 – 32.1 months) and was associated with biological equivalent dose (BED) over 90 Gy (p = 0.021) on univariate but not multivariate analysis. A BED of 90 Gy corresponds to 17.1 Gy delivered in one session, or 33.5 Gy delivered in 5 sessions assuming an alpha-beta ratio of 4 for breast carcinoma (1). Treatment related toxicity was marginal, with no Grade 3 or higher toxicities being reported by CTCAE v.4 criteria. For patients with HER2 positive lesions, intracranial control is particularly important due to their improved prognosis compared to other breast cancer subtypes (Table 1).

**Figure 1**




Combined Kaplan-Meier analysis showing OS, LC, and DIC for all patients.

## Conclusions

Frameless stereotactic radiosurgery is a safe and effective means of treating patients with breast cancer brain metastases. Early results suggest that durable intracranial control, both local and distal, in patients with breast cancer brain metastases can be achieved via a combination of WBRT and frameless stereotactic radiosurgery of greater than 90 Gy BED delivered to individual lesion sites with minimal toxicity. Due to the superior prognosis of this patient group compared to other patients with brain metastases multi-modal therapy is warranted in order to achieve lasting results.

## References

(1) START Trialists' Group, The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. Lancet. 2008 Mar 29;371(9618):1098-107.