Time-delayed Contrast-enhanced MRI Improves Detection of Brain Metastases: A Prospective Study for Validation of Diagnostic Yield

Jason P. Sheehan MD, PhD, FACS; Or Cohen-Inbar MD, PhD; Zhiyua Xu; Blair Dodson; Tanvir Rizvi; Christopher Durst; Sugoto Mukherjee MD

CNS 2016 ANNUAL MEETING San Diego CALIFORNIA SEPTEMBER 24-28, 2016

Introduction

The radiological detection of BMs is essential for optimizing a patient's treatment. This statement is even more valid when stereotactic radiosurgery (SRS), a noninvasive image guided treatment that can target BM as small as 1-2mm, is delivered as part of that care. The timing of image acquisition after contrast administration can influence the diagnostic sensitivity of contrast enhanced MRI for BM. We investigated the effect of time delayed acquisition after administration of intravenous gadolinium on the detection of BM.

Patient Related Parameters		
Parameter		**Value (n=no. of patients)**
Cohort size		**50**
Males: Females Gender		**50/50%** (n=25/25)
Age (years) at the time of MRI study (Median)		**60.5** (range 39-78)
Intracranial treatments prior to study MRI	Surgery (craniotomy)	**22%** (n=11)
	WBRT*	**34%** (n=17)
	SRS**	**56%** (n=28)
	Number of prior sessions (Median)	**1** (range 0-5)
Primary Tumor Histology	Lung (non-small-cell-carcinoma)	**44%** (n=22)
	Melanoma	**28%** (n=14)
	Breast adenocarcinoma	**18%** (n=9)
	Renal cell carcinoma	**2%** (n=1)
	Ovarian adenocarcinoma	**2%** (n=1)
	Seminoma	**2%** (n=1)
	Esophageal squamous cell carcinoma	**2%** (n=1)
	Cervical adenocarcinoma	**2%** (n=1)

Table 1

Table 2

Radiological Findings					
Radiological Parameter		**Neuro-Radiologist#1**	**Neuro-Radiologist#2**	**Neuro-Radiologist#3**	**Overall**
Non-Contrast No. of lesions (Median)		**1** (range 0-26)	**1** (range 0-24)	**1** (range 0-16)	**1** (range 0-26)
Contrast Time 0 Positive lesions (Median)		**3** (range 0-72)	**3** (range 0-65)	**3** (range 0-38)	**3** (range 0-72)
Contrast Time 10 Positive lesions (Median)		**3** (range 1-76)	**3** (range 1-67)	**3** (range 1-38)	**3** (range 1-76)
Contrast Time 20 Positive lesions (Median)		**3** (range 1-76)	**3** (range 1-67)	**3** (range 1-38)	**3** (range 1-76)
LMD*	Time-0	**14%** (n=7)	**0**	**24%** (n=12)	**19%**
	Time 10 min.	**16%** (n=8)	**0**	**26%** (n=13)	**21%**
	Time 20 min.	**16%** (n=8)	**0**	**26%** (n=13)	**21%**

*Leptomeningeal Disease

Methods

This is a prospective IRB approved study of 50 patients with BM who underwent post-contrast MRI sequences immediately after injection of gadolinium (0.1 mmol/kg Gadavist®) as part of clinical care (defined as t0), followed by axial T1 sequences after a 10 minutes (t1) and 20 minute delay interval (t2). MRI studies were blindly compared by 3 neuro-radiologists.

Table 3

Delayed MRI sequences Analysis				
Parameter			**Value (95% CI)**	**P**
Intraclass Correlation Coefficient (Single measures)		**T0**	0.914 (0.864-0.948)	<0.00005
		T1 (10 min.)	0.904 (0.848-0.943)	<0.00005
		T2 (20 min.)	0.905 (0.849-0.943)	<0.00005
Two tailed significance*	**Neuro-Radiologist #1**	T0 vs. T1		**0.039**
		T0 vs. T2		**0.016**
	Neuro-Radiologist #2	T0 vs. T1		0.096
		T0 vs. T2		**0.035**
	Neuro-Radiologist #3	T0 vs. T1		0.18
		T0 vs. T2		**0.034**

*Refer to the statistical analysis methods of the manuscript for further details

Results

Single measure intraclass correlation coefficients were very high (0.914, 0.904 and 0.905 for t0, t1 and t2 respectively), corresponding to a reliable inter-observer correlation. The t2 delayed sequences showed a significant and consistently higher diagnostic sensitivity for BM by every participating neuroradiologist as well as for the entire cohort (p=0.016, p=0.035 and 0.034 respectively). A disproportionately high representation of BM detected on the delayed studies was located within posterior circulation territories (compared to predictions based on tissue volume and blood-flow volumes).

Conclusions

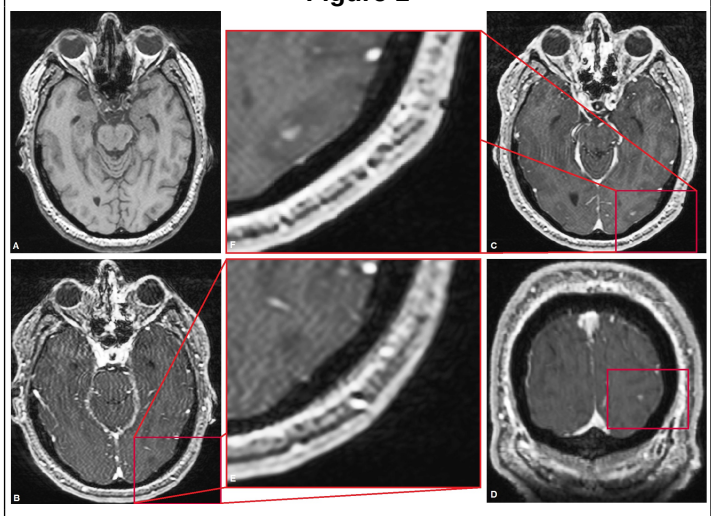
Considering the safe and potentially high yield nature of the delayed MRI sequences, it should supplement the basic MRI sequences in all patients in need of precise delineation of their intracranial disease.

Table 4

Patient and Tumor Features Correlation to Diagnostic Yield				
Parameter		**P**	**Hazard Ratio**	**95% Confidence Interval**
Patient Age (at time of MRI)		0.248	0.961	0.899-1.028
Prior WBRT*		0.531	1.587	0.374-6.737
Primary Histology	NSCLC vs. Other primary malignancies	0.911	0.923	0.225-3.780
	Breast Adenocarcinoma vs. Other primary malignancies	0.136	3.875	0.654-22.957
	Metastatic Melanoma vs. Other primary malignancies	0.297	0.407	0.075-2.199

*Whole Brain Radiotherapy

Figure 1



Sample patient. 58 years old with NSCLC. A, Axial non-enhanced T1WIMPRAGE, with no apparent lesions or edema. B+E, Axial gadolinium enhanced T1WI MPRAGE sequence at time-t0 (0-5 minutes after contrast administration), showing no apparent left occipital lesion (magnified in E) C+D+F, Axial (C+F) and coronal (D) Gadolinium enhanced T1WI MPRAGE sequence at 20 minutes delayed acquisition (time t-2) after contrast administration showing a definitive 4mm left occipital lesion.