Abstract
The development of metastases to the brain is a common and frequently devastating complication for patients with extracranial primary tumors. However, the generally poor prognosis of patients with brain metastases can be improved with early detection and treatment with stereotactic radiosurgery, as performed routinely at our institution. We have developed a novel small tumor detection algorithm based on 3-D template matching that will enhance the accuracy and efficiency of radiologists by allowing them to focus upon locations of high suspicion for metastatic brain tumors without having to spend time reviewing every image slice. Spherical tumor appearance models were created to match the expected geometry of the small tumors of interest and accounting for offsets due to the cut of MRI sampling planes. A 3-D normalized cross-correlation coefficient (NCCC) between the brain volume and spherical templates was calculated using a fast frequency domain algorithm. The data collected on 22 patient datasets consisting of 1320 coronal MR slices containing 161 total nodules shows that we can achieve currently a sensitivity of 87.6% with a false positive rate of 0.58 per image slice. Our results demonstrate that the 3-D template matching method can be an effective, fast, and accurate tool for automated detection of tumors in brain MRIs that can serve as a clinically useful tool to assist radiologists in providing earlier and more definitive diagnoses of metastases within the brain.

Introduction
Considerable mortality and morbidity can arise from the presence of brain metastases with patients most commonly presenting with headaches, seizures, or other neurological symptoms. However, a significant number of brain metastases are asymptomatic, at least initially, leading to belated detection and treatment and consequently, poorer prognosis. The accurate characterization of brain involvement is a critical factor in both the aggressive therapy regimens for good prognosis patients and the palliative control efforts directed at the brain metastases patients with terminal systemic disease. As a result, frequent screenings for brain metastases using high-resolution volumetric imaging must be performed in order to ensure appropriate treatment for all patients. This results in an ever-increasing workload for the radiologist, predisposing an increased tendency for reading error, especially for small nodules. Our automated 3-D template matching-based computer-aided detection (CAD) approach for metastatic brain tumors will address these issues of accuracy and efficiency by providing radiologists with locations of high suspicion for nodule presence.

Methods
The tumor detection components of this research are conducted entirely upon patient MR scans that have been accumulated previously at our institution. All anatomical MR scans that are used for metastasis detection were collected with a 1.5T GE Genesis Signa scanner and have an in-plane resolution of 0.43 mm and a slice thickness and separation of 2.5 mm. Prior to being subjected to the detection component of our algorithm, the brain mass is extracted from the skull and other non-brain soft tissue within each patient MR dataset using a semi-automated 3-D snake. Our detection algorithm employs the typical features of brain metastasis morphology through the use of a 3-D spherical template that incorporates a zero padding parameter to account for the well-demarcated nature of metastasis borders. Zero padding refers to the inclusion of a uniform number of zero intensity values around the border of the high-intensity spherical template. A normalized cross-correlation coefficient (NCCC) is utilized to identify the degree of similarity between the 3-D regions of the image and spherical templates of varying radii. Only image coordinates that generate an NCCC value above an experimentally determined threshold are identified as locations of potential brain metastases. This NCCC threshold value and the appropriate size for the zero padding can be selected on the basis of the results from a set of patient images utilized to optimize the balance between the algorithm’s sensitivity and false positive rate.

Results/Discussion
The major underlying hypothesis for our tumor detection algorithm is that a 3-D spherical template surrounded with a uniform layer of zero padding will correlate highly with the typical patterns of brain metastases on MR datasets. Normal anatomical structures such as cerebral blood vessels should be avoided as false positives in our final detection results due to poor matching of their 3-D branching with the zero padding parameter. In preliminary experiments, we found that we could detect the majority of brain metastases with our 3-D spherical templates while producing a minimal number of false positives. Figure 1 demonstrates the significant 3-D correlation that can be achieved between brain metastases and a spherical template of the appropriate diameter without also matching the surrounding extraneuse tissue. In order to establish the optimal settings for our template matching approach, a total of 22 patient datasets (1320 total coronal MR slices) were processed by our algorithm using 25 different combinations of zero padding size and NCCC threshold value. Figure 2 indicates that the optimal balance between sensitivity and false positive rate for these 22 datasets was achieved at a zero padding size of 0.86 mm and a NCCC threshold equal to 0.525 (indicated by arrow) where the overall sensitivity was 87.6% (141 out of 161 nodules detected) and the false positive rate was 0.58 per image slice.

![Figure 1.](image1.png) ![Figure 2.](image2.png)

Figure 1. [A, B] MR coronal image slices of extracted patient’s brain where locations of known metastases are indicated by circle. [A’, B’] Correlation maps at corresponding slice locations in patient image set where the gray-level values represent the 3-D normalized cross-correlation coefficient (NCCC) at each voxel between the 3-D spherical template and the 3-D patient image dataset.

Figure 2. Detection algorithm results combined from 22 patient datasets (1320 coronal MR slices with voxel size = 0.43 x 0.43 x 2.5 mm) containing 161 total brain nodules. Each of the 25 data points represent the sensitivity and number of false positives per image slices produced at one combination of zero padding size and normalized cross-correlation coefficient (NCCC) threshold value. NCCC threshold values of 0.550, 0.525, 0.500, 0.475, and 0.450 correspond to the first, second, third, fourth, and fifth points from left to right on each line of zero padding size, respectively.