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Fiducial-free Alignment Verification Techniques for Intracranial Radiosurgery

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Cover Page Footnote

I would like the thank Tom Lee, a senior software engineer at Optivus Proton Therapy, for his assistance with the Dicom medical image format. I would like to thank Dr. Keith Schubert, my advisor, for his guidance and the technical expertise he has provided throughout my research efforts, and I would like to thank Dr. Reinhard Schulte and Dr. Andrew Wroe for their medical expertise with which I have combined my technical experience to explore new opportunities. *The test image used in this research is copyrighted by the Massachusetts Institute of Technology and is used with permission.

Fiducial-free Alignment Verification Techniques for Intracranial Radiosurgery

Kenneth Williams

Abstract
The current process of intracranial radiosurgery treatment uses implanted titanium fiducials in the skull to assist in alignment of the patient. These fiducials add an element of physical and emotional stress to the patient, and scheduling the implantation procedures adds a delay of a few extra days before the radiosurgery procedure can begin. During the radiosurgery treatment, each proton beam is manually aligned by the therapist/physician with X-ray images and the fiducials that are visible on these images. This method of alignment can be time-intensive and requires personnel who are specifically trained in patient alignment. We propose a new method using image registration to automate this process in an effort to eliminate the need for surgical implantation of fiducials prior to treatment as well as to improve the accuracy and efficiency of alignment during treatment. Image registration is a technique used to align a moving image with respect to its known fixed image. Several methods of image registration are used for comparison: an enhanced correlation coefficient maximization algorithm, a mutual information maximization algorithm, and an extended phase correlation algorithm. Accuracy, robustness, and performance are emphasized in the comparison of these algorithms. Due to patient privacy, test images from MATLAB will be shown in this paper. This research was conducted under the clinical supervision of Dr. Andrew Wroe and Dr. Reinhard Schulte of the Loma Linda University Medical Center (LLUMC).

Author Interview

Which professors (if any) have helped you in your research?
Dr. Keith Schubert (With Dr. Andrew Wroe and Dr. Reinhard Schulte of LLUMC as clinical supervisors)

What are your research interests?
Medical imaging and software engineering

What are your plans after earning your degree? What is your ultimate career goal?
I plan to work with Loma Linda under a grant before pursuing my PhD. I would like to become a professor to assist students pursuing research in computer science as applied to the medical field.

Acknowledgements
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Keywords: *Skull Alignment, Radiosurgery, Image Registration, Enhanced Correlation Coefficient, Mutual Information, Iterative Closest Point, Phase Correlation*

Introduction

The current process for alignment during radiosurgery utilizes titanium fiducials that are implanted into the patient's skull during a surgery scheduled prior to treatment. During treatment, each proton beam is manually aligned by the therapist or physician with digital X-ray images and the fiducials that are visible on these images. The focus point at which the beam's dose is the greatest, known as the Bragg peak, is a phenomenon exploited by proton radiation therapy for cancer to concentrate the effect of the proton beams on the tumor while minimizing damage to critical structures and other healthy issue within the patient undergoing treatment. This peak in the proton's dose distribution occurs because the interaction cross section increases as the energy decreases. To maximize the effectiveness of the Bragg peak, the patient must be aligned properly for accurate targeting of the tumor volume. This process can be time consuming, therefore in an effort to reduce unnecessary delays caused by the fiducials as well as increase efficiency of this process, Dr. Andrew Wroe and Dr. Reinhard Schulte of LLUMC have expressed the desire to research new methods of skull alignment for intracranial radiosurgery.

Background

Stereotactic radiosurgery is a treatment that uses focused beams of radiation, either with gamma rays, X-rays, or protons, to treat cancerous tissues without a surgical incision or opening. The form of radiosurgery for which this research is intended uses a proton beam to treat the patient. Proton beam therapy uses a particle beam for its treatment rather than rays of radiation. The beams are focused on an intended volume of cancerous tissue by utilizing what is known as the particles' Bragg peak. This peak occurs on the Bragg curve, named after its discoverer William Henry Bragg in 1903, which is a graph that plots the loss of energy of ionizing radiation during its traversal through matter. This peak occurs just before the particles come to rest. To effectively utilize the Bragg peak, both the patient and the beam must be accurately aligned so that no healthy tissue or critical structures within the patient are damaged. This research focuses on the alignment of the patient during the radiosurgery treatment.

Purpose

We propose a new method for skull alignment using image registration. This will eliminate the need for the implanted fiducials and further automate the alignment process during treatment which will provide benefits with respect to accuracy and efficiency over the current methods of alignment. Another aspect of reducing the delays caused by the surgery to implant the fiducials is the potential ability to eliminate any further growth of the cancerous tissue before the treatment occurs. The total duration of the current process is estimated to last up to one month, including surgery to implant the fiducials into the patient's skull, patient imaging, treatment planning, calibration, and the radiosurgery treatment itself. By automating this process using image registration methods and removing the need for the implanted fiducials, the length of time for this process can be reduced to approximately one week.

Image Registration

Image registration is the process of transforming a captured image in order to align it with its known reference image. While the various papers discussing the image registration methods used in this paper refer to these images by different names, these images will be referred to in this paper as the moving and fixed images, respectfully. Image registration is useful for automating skull alignment for radiosurgery to significantly reduce delays throughout the treatment process and greatly increase its efficiency. Many applications for image registration exist, therefore the first step of registration is to determine the type of transformation that models the mapping of the fixed and moving images. As the skull does not have a tendency to become warped in the given time frame of the procedure for radiosurgery nor does this time frame allow for the skull to grow by any significant amount, the algorithms used in this procedure only need to take into account rigid transformations, which include the rotation and translation of the images. As the fixed and moving images are captured using different devices, the algorithms must take into account a multimodal image capture modality, as well as the noise and difference in illumination between the two images. Methods of image registration compared in this thesis include a forward additive enhanced correlation coefficient maximization algorithm (Evangelidis & Psarakis, 2008), a mutual information maximization algorithm (Mattes, Haynor, Vesselle, Lewellen, & Eubank, 2001), and a log-polar fast Fourier transform-based phase correlation method (Reddy & Chatterji, 1996). Given the sensitivity of the application regarding its use in the treatment of a patient, the image registration method(s) must fulfill basic requirements in accuracy, robustness, and performance.

Enhanced Coefficient Correlation Maximization

The enhanced correlation coefficient method maximizes the linear dependence between the fixed and moving images in order to achieve the optimal alignment. This algorithm uses an iterative forwards additive approach to determine the alignment, sacrificing low computational complexity, in comparison to alternative versions of this method, for more accurate results (Evangelidis & Psarakis, 2008). The difference from other methods using this metric, such as an inverse compositional method, is that the forward additive approach uses an approximated parameter vector that is optimized each iteration until its norm becomes smaller than a predefined threshold.

The enhanced correlation coefficient maximization algorithm begins with initializing a warping transformation matrix using a given initial estimate. Next, the algorithm defines a region of interest, which in our case just ignores a margin of the image of five percent of the mean of the height and width of the image. Using the initial transformation estimate, the moving image is warped and the zero-mean vectors are compared using a pre-defined threshold. This process repeats until the allotted amount of iterations and pyramid levels have been exhausted or the alignment has been determined optimal.

This algorithm is beneficial for this application as it is known for its robustness regarding noisy conditions and photometric distortions in contrast and brightness as well as a statistical robustness against outliers. However, this method has disadvantages that must be considered, including its computational complexity and the fact that it does not imply causality. Uncorrelated variables may not necessarily be independent, which means two uncorrelated images may still be related by a particular transformation that this method was unable to determine.

This algorithm was chosen for this research as it has already been shown to be superior to similar algorithms such as the Lucas-Kanade and Simultaneous Inverse Compositional registration methods (Evangelidis & Psarakis, 2008). While two versions of this method were introduced, for simplicity only the forward additive version is used.

Mutual Information Maximization

Mutual information is a statistically-based metric derived from probabilistic measures of image intensity values (Mattes, et al., 2001). This algorithm uses the joint probability distribution of a set of pixels from the fixed and moving images to iteratively measure the certainty that the set of pixels from one image map to a set of pixels to the other image. The probability distributions are based on marginal and joint histograms of the fixed and moving images. Higher mutual information implies lower uncertainty, thus also implying the images are more likely aligned than previous iterations. This algorithm uses a specified number of samples used to compute the probability density estimates and the number of bins used to compute the uncertainty. The joint probability density function is then evaluated at each bin using the samples, while entropy is computed by summing over the bins. Zero-order and third-order B-spline kernels are used to compute the probability density functions of both images.

Mutual information maximization is a direct measure of the probabilistic relationship of two random variables, which implies that if two images do not share mutual information, then they are not related by a particular transformation. This allows the algorithm to determine that two images cannot be aligned. Like the enhanced correlation coefficient maximization algorithm, mutual information maximization is also computationally intensive. Another drawback to this method is that an increase in noise results in a decrease in mutual information, thus finding an optimal alignment is more difficult.

Log-Polar Fast Fourier Transform / Phase Correlation

The frequency domain approach used in this research extends the phase correlation technique to find simple transformations such as rotation, translation, and scale by converting the fixed and moving images to log-polar coordinates (Reddy & Chatterji, 1996). This algorithm differs from intensity-based or feature-based algorithms as it uses properties of the Fourier transform to find the optimal alignment. Benefits of this algorithm include robustness against noise, low computational cost, and rotation and scale can be found invariant to translation. Note, however, that scaling is ignored in this research as a patient's skull will not expand within the time frame for the radiosurgery treatments.

First, the fast Fourier transform of the fixed and moving images are taken and then converted into log-polar coordinates. Another fast Fourier transform is calculated before computing the phase correlation between the two images. The peak of this phase correlation provides the angle of rotation of the moving image from its fixed image. Similarly, this process is repeated outside of log-polar space to obtain the translation in the x and y directions. The peak in this case is the location in the phase correlation matrix of the maximum value. The order in which the angle of rotation and the translation values are calculated is not pertinent and can be reversed from this process. The ability to change the order in which these transformations are calculated lends itself to parallelization of the algorithm which can further increase its efficiency.

Unlike the previously discussed algorithms, fast Fourier transforms are computationally efficient. This algorithm is also highly resilient to noise and allows rotation to be found invariant to translation, which allows for both transformations to be determined in parallel. A disadvantage to this method is that performance is reduced if the shift is linear, as opposed to circular. A circular shift, in the context of image manipulation, essentially wraps the portion of an image that would be shifted out of the original boundaries of the image to its opposing region of the image. For example, given a downward shift of ten pixels, the bottom ten pixels of the shifted image would be moved to the top of the image.

Data

The first iteration of this research was conducted using test images from MATLAB. Due patient privacy regulations, we opted to show the test images for this paper instead of Dicom images of a patient's skull. The original test image acts as the fixed image, while the moving image is derived from the fixed. To obtain the moving image, the fixed image is rotated six degrees in the counter-clockwise direction and a translated ten pixels to the right and ten pixels downward. See Illustration 1 for the input images used to compare each algorithm.

Illustration 1: Input Fixed and Moving Images

Results

The results of the three algorithms – enhanced correlation coefficient (ECC) maximization, mutual information maximization, and log-polar fast Fourier transform (FFT) based phase correlation – are as shown in Table 1. Each algorithm is implemented using MATLAB and its run time is calculated using MATLAB's built-in stopwatch timer. The angles of rotation are in degrees, the translations in X and Y are in pixels, and the values of time are in seconds. The fixed and aligned moving images are also shown in an overlay fashion to visually demonstrate the accurate of each algorithm.

	ECC	Mutual Information	FFT
Angle of Rotation	6.000218	6.221918	5.625
X Translation	10.00038	8.849472	10
Y Translation	9.999519	10.78977	10
Execution Time	2.5464	2.4900	0.2219

Table 1: Registration Results

Illustration 2: ECC Registration

Illustration 3: Mutual Information Registration

Illustration 4: FFT Registration

The included illustrations show the alignment of the moving image onto its fixed image for each algorithm. The green and purple overlays indicated the difference between the moving and the fixed images, respectfully. The enhanced correlation coefficient maximization image result is noteworthy as the green overlay is much larger than that of the other two illustrations. This is due to the algorithm's nature of sub-region mapping as opposed to the algorithm aligning the entire image at once.

To calculate the error, each calculated rotation and translation value from the Table 1 is compared to the known respective values for rotation and translation in the x and y directions from which the moving image was produced. The errors in percentages are shown in Table 2.

	ECC	Mutual Information	FFT
Angle of Rotation	0.003633%	3.698633%	6.25%
X Translation	0.003799%	11.50527%	0%
Y Translation	0.004810%	7.897700%	0%

Table 2: Registration Error

Conclusions

The gradient-based forward additive enhanced correlation coefficient algorithm provides the most accurate angle of rotation, while the frequency-based Fourier transform provides the most accurate translations in the x and y directions. The fastest overall algorithm is the Fourier transform algorithm. The mutual information algorithm did not provide any significant benefits in accuracy or performance over either the enhanced coefficient correlation maximization algorithm nor the fast Fourier transform phase correlation algorithm. Refer back to Illustration 2 for image results of the enhanced correlation coefficient maximization algorithm, Illustration 3 for image results of the mutual information maximization algorithm, and Illustration 4 for image results of the fast fourier transform-based phase correlation algorithm.

Given our results, the mutual information maximization algorithm can be ruled out as insufficient for our purposes due to its low accuracy in comparison to the other two algorithms, while the results of the Fourier transform and the forward additive enhanced correlation coefficient algorithms are much closer with respect to accuracy. They both provide fairly accurate results, and considering the current methods of skull alignment take time on the order of minutes, the longer execution time of the enhanced correlation coefficient algorithm is negligible. Due to the similar accuracy of the Fourier transform and ECC algorithms, these algorithms will be considered for parallel calculations during treatment and determined on an individual treatment basis.

Future Work

Another algorithm to be considered for future work for this research is a feature-based algorithm using an iterative closest point technique. This method is an iterative process that works in two steps. Each iteration first matches points based on the latest transformation estimate and then refines the estimate based on the matches. Normally, this algorithm requires a good initial estimate for the overall image, however, the dual-bootstrap method (Stewart, Tsai, & Roysam, 2003) requires the initial estimate to be accurate only over a sub-region of the image. During each iteration of this algorithm, the region over which the model is accurate, the bootstrap region, and the chosen transformation model are expanded until the bootstrap region fits the entire image.

While computationally efficient, this algorithm is prone to accumulative errors as each iteration heavily relies on the calculated transformation of the previous iteration. This drawback explains the requirements of an accurate initial estimate. Beyond this disadvantage, any further disadvantages are yet to be seen regarding how it compares to the previously tested algorithms.

Upon finalization of this research, including fine-tuning of the image registration algorithms, pre-conditioning of the fixed and moving images in order to approach ideal conditions under which the algorithms operate optimally, and exhaustive testing to include various conditions of noise and geometric and photometric distortion to verify which algorithms provide optimal accuracy, efficiency, and robustness, this research will be used to treat patients undergoing radiosurgery. If a particular algorithm outperforms all of the tested algorithms in all conditions, it will be solely implemented into the Odyssey treatment planning software developed by Optivus Proton Therapy, Inc. which is currently used by LLUMC. If multiple algorithms prove optimal for certain conditions, they will be implemented in a parallel, tournament-style approach in order to determine the most accurate alignment.

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