# Quantification of Mural Thrombi with a Fibrin-Specific MRI Contrast Agent using an Image Segmentation Algorithm

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## Introduction

Image segmentation has frequently been used as a means to quantify regions of tissue. While a simple thresholding scheme is sufficient for many purposes, it is not robust in most MR applications due to locally-varying image intensities. In this work, automated iterative thresholding was used to segment thrombi from 3D MR images of carotid arteries in rabbits. Contrast was provided by the fibrin-specific gadolinium-based contrast agent EP-2104R (EPIX Medical, Cambridge, MA). The agent provided sufficient contrast to quickly quantify thrombus volumes with minimal input.

## Materials and Methods

Twelve (12) white New Zealand rabbits were anaesthetized and mural thrombus was induced in the right carotid artery by crush injury. 4/4/4 rabbits received a 1/2/5 μmol/kg IV dose, respectively, of EP-2104R. Approximately 35 minutes after injection, spoiled gradient echo images were acquired at 1.5 Tesla in three dimensions. Fat suppression and inferior/superior inflow suppression were used. Image parameters were: $T_R$ / $T_E$ / flipangle = 40 ms / 4 ms / 40º. Sixty 1.2 mm axial slices were acquired with an in-plane resolution of 0.31mm. The rabbits were sacrificed after heparin administration to stop coagulation *post mortem*. The affected carotid arteries were excised, and the thrombi were extracted from the vessels and weighed.

All images showed obvious contrast at the interface of the vessel wall and lumen in the area of injury. Before analysis, the image stack was interpolated to 0.6mm slice thickness, and each slice was rendered at 6x resolution using bi-cubic interpolation. An algorithm was developed which took as its inputs an expert-picked region of background muscle, and a point in the enhanced region. The initial threshold level was defined as a pixel value two standard deviations above the mean background region (BR) pixel value. The region of interest (ROI) was defined as the continuous 3D region that contained the expert-picked point. The threshold level was automatically adjusted until the mean and standard deviations of the pixels in the ROI and BR satisfied a t-test for dissimilarity at the $p < 0.025$ level. The mean pixel values of the BR and ROI were recorded, as well as the ROI volume. The "signal intensity ratio" (SIR) was taken to be the ratio of mean ROI to mean BR intensity. The "enhancement index" (EI) was defined as the ROI volume times the SIR. Total Gd (femtomoles) was measured by inductively coupled plasma-mass spectrometry (ICP-MS) was compared to EI measured using the image segmentation method.

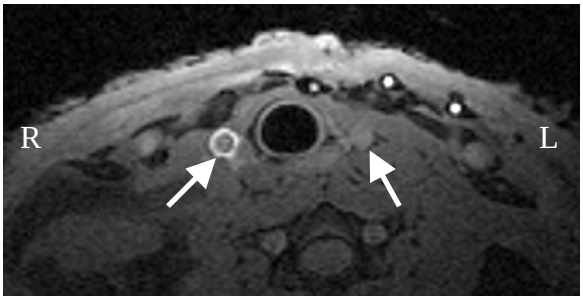


***Figure 1.*** *Image after 5 μmol/kg EP-2104R. The injured right and normal left carotid are indicated.*

## Discussion

The results indicate that the fibrin-targeted agent provides sufficient contrast for robust segmentation of MR image data. The thrombus volumes extracted with the segmentation algorithm correlated well with weights of extracted thrombi, suggesting that the combination of targeted contrast and appropriate image processing tools may facilitate quick and robust quantification of thrombi *in vivo*. Such quantitation may be valuable in a wide variety of applications, including measurement of total thrombus burden and identification of total volume of thrombus associated with ruptured vulnerable plaque.

## Results

The SIR scaled with dose. The regions were, however, robustly segmented at all three doses. Across thrombi in all 12 animals, the EI showed excellent correlation with total gadolinium uptake, r = 0.95. The volume of ROIs correlated well with the measured thrombus weights, r = 0.87 (see Figure 2). This correlation does not appear to be dose-dependent in the range studied.

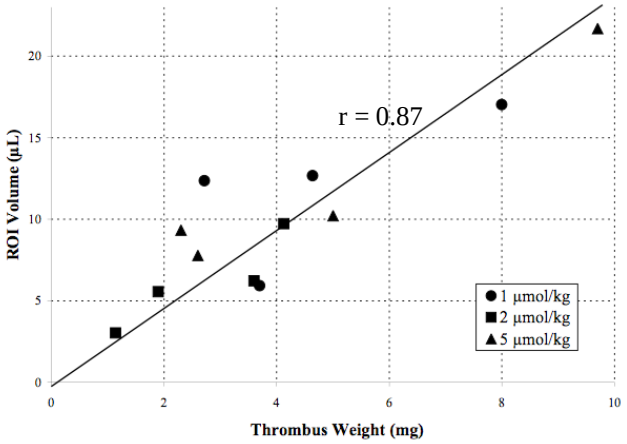


***Figure 2.*** *Thrombus weight vs. volume measured by the image segmentation algorithm.*