Atherosclerotic carotid plaque might rupture without warning causing fatal events. Currently, plaque vulnerability assessment is based mainly on medical images and experience from physicians. However, both morphological information and mechanical forces should be considered in an integrated way for a better diagnosis. MRI-based computational models with fluid-structure interactions for human atherosclerotic carotid plaques were developed to perform mechanical analysis and quantify critical stress conditions related to plaque rupture. A critical site selection method to quantify critical stress was proposed. In vivo MR-images from 6 patients (3 ruptured plaques with ulcer and hemorrhage, 3 non-ruptured) were used. Proper circumferential and axial shrinking was performed to get the start shape for the numerical model. Results indicated that critical stresses from plaques with ulcer were significantly higher than the non-ruptured ones. Large scale patient-specific studies are needed for further validation of our method and findings. Acknowledgement: This research was supported by NSF grant DMS-0540684 and NIH grant R01 EB004759. MRI data was provided by Dr. Chun Yuan’s group in University of Washington. (Received September 01, 2008)