We present a method to optimize Gamma Knife™ (Elekta, Stockholm, Sweden) radiosurgery treatment planning. This device applies radiation to brain tumors in a series of small egg-shaped “shots”. A Guided Evolutionary Simulated Annealing based optimization algorithm is used to maximize the therapeutic benefit through a probability model that indexes voxels within a patient volume image as: normal, critical normal tissue, or tumor tissue. Our evolutionary strategy varies according to the size and complexity of the tumor. Indices of dose conformality, level, and homogeneity are utilized as criteria to evaluate the degree to which a treatment plan has been optimized. Two examples compare the GESA algorithm with the manual methods currently used by clinicians. GESA improves treatment planning over the treatment team’s manual effort. We also indicate that for a treatment plan with more than 8 shots, initial seeding (shot number, size, position, and weight) via medial axis significantly reduces computation time.