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The overall quality and accuracy of patient treatment in radiation therapy is determined by the interaction between the complex technical tasks of clinical decision making, simulation, treatment planning and treatment delivery which constitute the “treatment process”. The technical tasks related to each of these areas are typically performed by different sets of people, which creates the potential for sub-optimal and compromised treatment quality. The increasing use of 3-D conformal and IMRT treatments, with the associated conformal radiation fields and high dose gradients presents the potential for geometric misses and dosimetric errors, which will compromise patient outcomes. This work examines the role of process management using the six-sigma approach in optimizing and controlling the quality of these highly technical treatments. A comprehensive map of the “treatment process” starting with simulation and ending with treatment is developed for several treatment sites. Variables in the process influencing treatment quality, and potentially patient outcomes, are identified. Sources of uncertainties in these variables are identified, their relative importance and magnitude is estimated, and ways of reducing them are explored. The role of quality control checkpoints at different steps in the process is examined for value and efficiency. The technical goal of the six-sigma approach is to reduce the variance in a process to the sixth standard deviation. The economic and technical feasibility of such a goal and its expected impact on patient outcomes is analyzed.