To determine if margins are adequate or excessive for any particular site in external beam radiation therapy, it is necessary to understand the various uncertainties that need to be taken into account. One of these factors is patient setup error. We measured the frequency and magnitude of setup errors in patients undergoing conformal radiation therapy for non-small cell lung carcinoma. Setup errors were measured by using a software tool to compare contours of the same landmarks drawn on digitized portal and simulator images for each field. However, the choice of anatomic landmark can influence the size of the setup error measured. Thus, our study consisted of two components: (a) an analysis of movement of landmarks due to breathing and other patient motion by review of video tapes of fluoroscopy from simulators and (b) application of this information to measure setup errors by comparing digitized portal and simulator films using stable landmarks (i.e. those showing minimal intra-fractional motion). We found that intra-fractional movement of some landmarks was comparable to or larger than the setup errors; the latter determined from landmarks showing little movement. Results on intra-fractional motion of landmarks in the thorax for a group of patients will be presented as well as information as to how the choice of landmarks affects determination of the setup error.