**Purpose:** To develop algorithms that can track the invisible lung tumors by tracking relevant anatomic features in the fluoroscopic images based principle component analysis (PCA) and regression analysis.

**Method and Materials:** For each patient 15 seconds of fluoroscopic images were taken before treatment and used as training dataset. A few regions-of-interest (ROIs) were manually selected in the first image frame that may contain anatomic features correlated with tumor motion. PCA was applied to reduce the dimensionality of each ROI to 3. Tumor positions were manually marked by an expert observer in all training images. Regression methods were applied to build the correlations between the tumor position and the PCA-processed ROIs. Then the correlations were used to predict the tumor positions in the testing images. Four regression methods were considered: 1-degree and 2-degree linear regression, artificial neural network (ANN), and support vector machine (SVM). Their accuracy was assessed by comparing the prediction results with the reference tumor locations manually determined by the expert observer.

**Results:** 12 sequences of fluoroscopic images have been studied retrospectively. Results are reported in terms of mean and variation of localization error. Considering all regression methods, the mean localization errors (MLE) are smaller than 1 mm for most patients and in the worst case is still smaller than 2.5 mm. Variations are smaller than 1 mm most of the time, and the largest variation is about 9 mm. 1-degree linear regression and ANN in general perform better than the other two methods. The other two methods tend to have overfitting problems.

**Conclusion:** Based on PCA and regression analysis, we proposed a novel method that can track the invisible lung tumor in fluoroscopic images by tracking correlated anatomic features. The method has an accuracy of 1mm in most of cases and smaller than 3mm in the worst case.