Purpose:
To present a method for image comparisons and detection of statistically significant differences (SSDs) between medical images that contain a significant amount of noise, where standard similarity measures like mutual information do not work very well.

Methods:
The basic idea is that if there are two noisy images which contain SSDs, these differences will appear as outliers in the distribution of pixel intensities in the difference image. Therefore, the method applies a statistical test and identifies the outliers found as SSDs. The tests for outliers are applied on the entire difference image (global approach), on a part of the image around a tested pixel (local approach), or both (mixed approach). The mixed approach first uses a global approach to exclude a set of outliers before invoking the local approach. For performance assessment, the algorithm is applied to synthetic image pairs with known noise levels and SSDs. It is also tested on PET images reconstructed with different algorithms from the STIR package using sinograms obtained from MC PET simulations using egs_pet, on electron beam dose distributions computed with the VMC++ code, on CT and SPECT images.

Results:
Best performance is achieved with a mixed approach. For the synthetic images the mixed approach identifies SSDs that are larger than four standard deviations of the noise. Visible differences between pairs of PET, CT, SPECT and dose distribution images are also successfully identified.

Conclusions:
A new method for automatic detection of significant differences between noisy medical images is presented. The method has potential for application in situations where a quantitative comparison and identification of regions of differences is difficult or not possible due to the presence of significant amount of noise. The algorithm is applicable to PET, SPECT and CT imaging as well as to problems related to comparisons of dose distributions.

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