

# Detection of MS Lesions in MRI Scans using Non-Parametric Image Subtraction

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## Abstract

MS lesions can be detected by simple subtraction of MRI scans taken before and after the injection of GdDTPA contrast agent. However, this highlights global changes in the post-injection scan in addition to the lesions. We introduce a new non-parametric subtraction measure, analogous to standard statistical tests, which allows a direct probabilistic interpretation of image differences. We demonstrate the technique using scans of MS lesions, but we expect it to be applicable to a wide range of image formation processes.

## Method

Non-parametric image subtraction [1] measures the differences between an image pair in terms of an implicit model of the data behaviour. This is obtained in the form of a scattergram  $S(g_1, g_2)$  of the grey levels  $g_1, g_2$  of corresponding pairs of pixels. A vertical slice in the scattergram  $F(g_1 = \text{const}, g_2)$  isolates all pixels in image 1 with some grey level  $g_1 = \text{const}$ . The distribution of this data gives the relative frequency of grey levels for the corresponding pixels in the other image. Normalisation converts these frequencies into probabilities. An integration is then performed along the vertical slice passing through the coordinates defined by each pixel pair, summing all smaller probabilities. This is directly equivalent to the construction of a confidence interval [2], giving the probability of finding a more uncommon pairing of grey-levels than that seen at the original pixel pair. This probability can then be used to produce a statistical difference map.

The distribution of grey levels in the difference image is by definition uniform (and therefore honest), providing a mechanism for self-test. In addition a standard equation,

$$p' = p \sum_{j=0}^{n-1} \frac{(-\ln p)^j}{j!} = \frac{\Gamma(n, -\ln(p))}{\Gamma(n)}, \text{ where } p = \prod_i \omega_i, \quad (1)$$

exists to renormalise any quantity  $p$  that is the product of  $n$  independent quantities  $\omega_i$ , each having a uniform distribution, such that  $p'$  also has a uniform distribution. Non-independent quantities can be combined by introducing the concept of an effective number of degrees of freedom, using the expression for  $p'$  in terms of gamma functions to extend the definition to non-integer values of  $n$ . The product of each pixel in the difference image with its four nearest neighbours can be treated in this way. Localised difference regions are manifested as clusters of low probability pixels, and so will form very low probability products that do not renormalise correctly. The probability distribution for the renormalised image will therefore be uniform for background pixels, but will feature a spike close to zero for localised difference pixels. This spike can be extracted using thresholding, allowing volumetric analysis of the image differences.

## Results

The subtraction technique is non-symmetric under interchange of image data: it identifies localised differences only in the image plotted on the ordinate of the scattergram. Therefore, subtractions between pre and post contrast scans taken at a single visit show all highlighted tissues (enhancing MS lesions, vasculature), whereas subtractions between post contrast scans from different visits identify only newly enhancing tissue in the image on the ordinate.

The new technique was tested on T1 weighted pre and post GdDTPA contrast scans of a single MS patient, taken during five visits spanning approximately five months (only a few examples

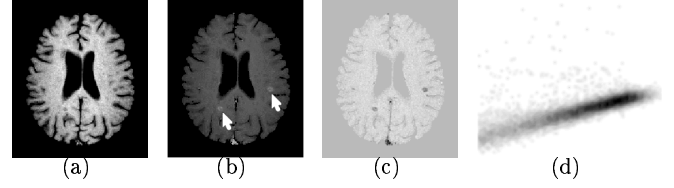


Figure 1: Pre-contrast (a), post-contrast (arrows show lesions) (b), simple subtraction (c) and scattergram (d).

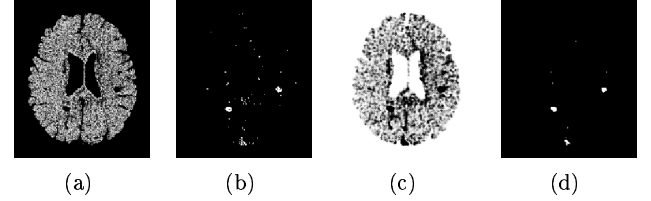


Figure 2: NPI subtraction (a), threshold at 1% (b), 5x renormalisation (c) and threshold at 0.001% (d).

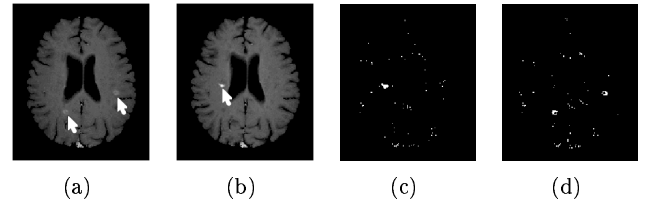


Figure 3: Post contrast scans from two visits (arrows show lesions) (a,b); NPI subtraction b-a, thresholded at 1% (c); same for a-b (d).

are shown here). Fig. 1 shows pre and post contrast scans showing two MS lesions, taken at the same visit, together with the result of simple subtraction and the scattergram for this image pair. Fig. 2 shows the result of the new subtraction technique for these images, together with a thresholding to highlight the low probability regions. The lesions and vasculature are clearly identified. Applying the five-way renormalisation technique (Fig. 2c) allows extraction of the lesions at lower thresholds (Fig. 2d), and also eliminates much of the (single-pixel) vasculature.

Fig. 3 shows subtractions between post-contrast scans taken during visits separated by approximately two months. As stated above, enhancing tissues present only in the second scan (Fig. 3c), or only in the first (Fig. 3d), can be identified. These subtractions clearly show the changes in the enhancing lesions, together with some small contamination from vasculature.

## Conclusions

The detection of MS lesions in MRI scans is an important issue both in relation to monitoring the progress of the pre-clinical disease and to therapeutic trials [3]. Currently the most popular technique used for this purpose is visual inspection of the scans. We have presented a novel image subtraction routine based upon conventional statistical approaches which can identify small but significant differences between an image pair in a robust manner, producing an output in terms of a probability. We have demonstrated the use of this measure in automatic identification of MS lesions, but expect it to be applicable to a wide range of image formation processes.

## References

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2. J. Neyman, *Phil Trans Roy Soc Lond A236*, 333-380, 1937.
3. Wolansky L J, et al. *Journal of Neuroimaging 4(3)*, 141-145, 1994.