Unifying lesion masking and tissue probability maps for improved segmentation and normalization

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INTRODUCTION

With SPM, "Unified Segmentation" (US) is the usual approach to warp brain images into a standard reference space, i.e. perform spatial normalization, and derive posterior probability maps of the brain tissues [1]. The US approach relies on a spatial deformation model and prior "tissue probability maps" (TPM) of the head tissues.

When dealing with data from patients with focal brain lesions, e.g. tumors or multiple sclerosis (MS) lesions, US does not work because it cannot account for the abnormal tissue distribution. A common work around is the "cost function masking" (CFM) approach [2,3] where the region of abnormal tissues is masked out from the processing using a (manually) pre-defined binary mask of the lesion [6,8].

Here we extend the US approach to provide a more principled solution for brain images with focal lesions. The aim is twofold:

1. **a more accurate warping into the reference space of the healthy tissues allowing further inter-subject comparisons, and**
2. **an updated more precise delineation of the lesion(s) through *a posteriori* probability map of lesioned tissues.**

METHODS

First one needs to produce an approximate map of the lesioned area(s), aka. a lesion mask (manually or through some algorithm). Then we modify the standard TPM by adding a subject-specific "lesion probability" map [5,7], in 2 steps:

1. "Masking & US", i.e. estimate a preliminary spatial warping from subject to MNI space with the "cost function masking" approach applied on one anatomical MRI (typically T1-weighted) and the (slightly enlarged) approximate lesion mask

   → **MNI-warped approximate lesion mask**

2. "TPM updating", i.e. build the TPM-with-lesion based on the type of lesion and healthy tissue class(es) affected, e.g. WM-only for a MS patient:
   i. add a new tissue class for the lesion, defined from the smoothed MNI-warped approximate lesion mask to the standard healthy TPM, accounting for the prior probabilities of the affected tissue class(es);
   ii. update the healthy tissue class(es) affected by the lesion.

   → **Subject specific TPM-with-lesion**

Finally the TPM-with-lesion is fed into the US with the patients anatomical MR image(s). If multiple contrast images (T1, T2, PD, Flair,…) are available, then multi-channel segmentation is performed.

→ **Deformation field, accounting for the *a priori* focal abnormal tissue (lesions) + posterior probability maps for healthy & lesion tissue classes.**

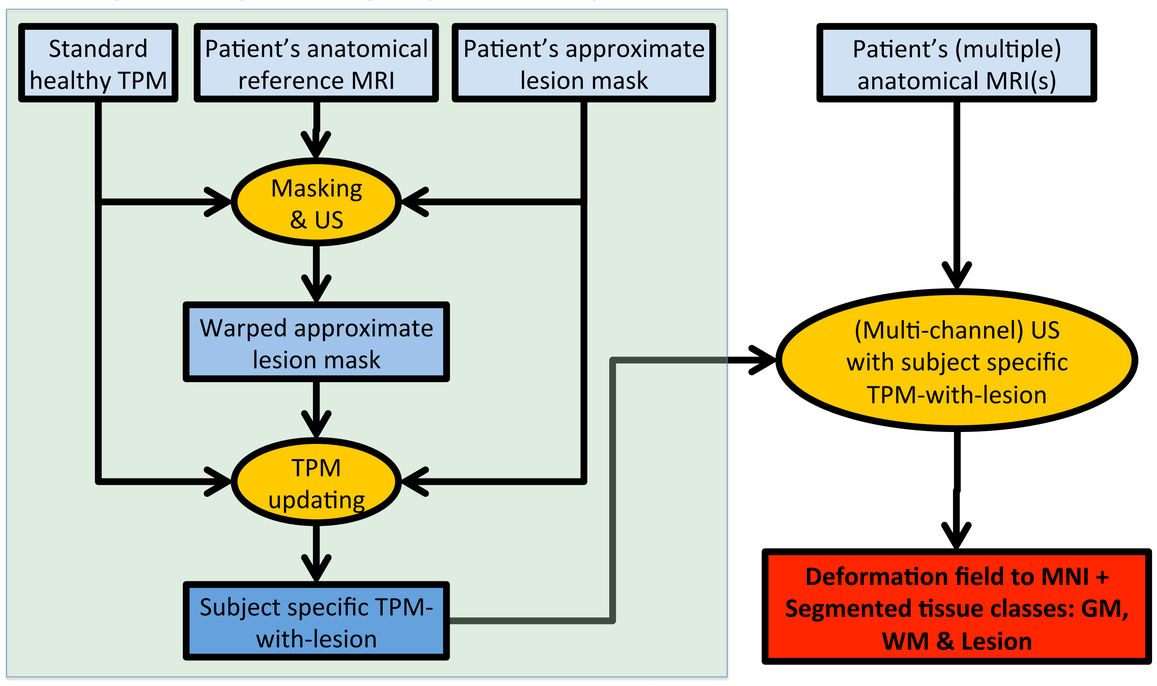

Fig. 1. Workflow of the "Unified Segmentation with Lesion" (USwL) approach. The green box summarizes the creation of the subject-specific TPM-with-lesion. Note that the implementation of the US algorithm is the one from SPM12 without any modification, only the TPM (and associated parameters) are adapted.

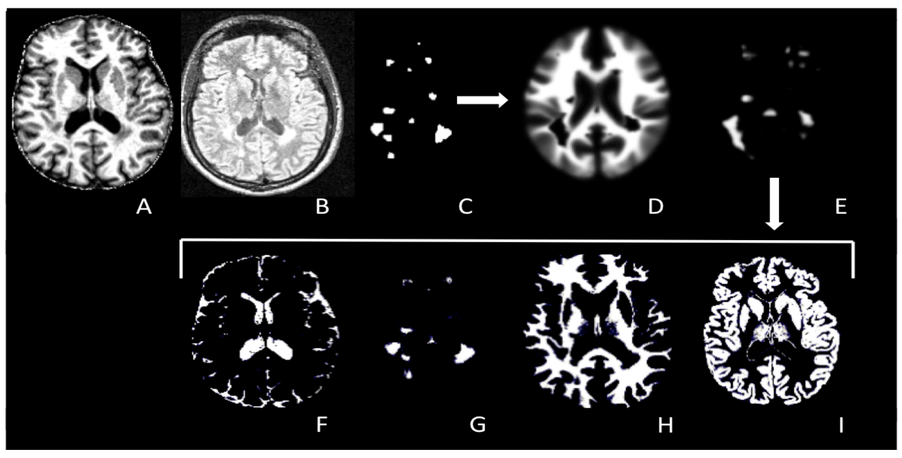

Fig. 2. Example of USwL application on a MS patient (data from the GIGA-CRC). (A, B) MT and FLAIR-weighted MR images; (C) approximate binary lesion mask; (D, E) updated WM and lesion prior probability maps; (F-I) *a posteriori* probability maps for CSF, lesion, WM and GM tissue classes.

CONCLUSION

We developed and tested a new tool for US that allows to include focal lesions in the mix of tissue classes. Over the 2 datasets considered, USwL demonstrated improved performances compared to the standard CFM-US approach.

Simply starting with an approximate lesion mask, we observed:

1. a **more accurate warping** into the reference space of the healthy tissues, and
2. a **more precise delineation of the lesion**(s).

The whole code will be made available as an SPM add-on toolbox (via MatlabBatch interface) on

https://github.com/CyclotronResearchCentre/USwithLesion.

RESULTS & DISCUSSION

An example of our USwL approach is presented in Fig. 2. USwL was also tested and on 2 publicly available datasets:

1. the '**Multimodal Brain Tumor Image Segmentation Benchmark' (BRATS)** [4] which includes T1 and FLAIR images of 30 patients with gliomas and their annotated tumor mask. The latter are further considered as the ground truth.
2. the **'MS lesion segmentation challenge'** (**MSchal**) [8] which includes T1, T2 and FLAIR images of 20 patients with MS as well as the manually annotated lesion. Because of their low quality, the latter are further considered as only approximate here.

For each subject of the **BRATS dataset**

- a rough lesion mask is manually build from the FLAIR image using MRIcron.
- USwL is used to segment the pair of T1 and FLAIR images along with this approximate mask, assuming that all GM, WM and CSF tissue classes could be affected by the lesion.
- the posterior probability map for the lesion tissue is cleaned up (preserving the bigger clusters) and thresholded.

Overall the USwL improved ($p<.05$) the similarity of the lesion mask to the annotated tumor, in term of voxel matching (sensitivity, specificity & Jaccard coefficient).

Synthetic lesioned brains were also generated to assess the quality of the deformation for the healthy tissues, indicating the superiority ($p<.05$) of the USwL compared to the standard approach.

For each subject of the **MSchal dataset**

- USwL is applied on the 3 structural MR images with the lesion mask provided. The lesion is constrained to be only in the WM, as is plausible with MS).
- the posterior probability map for the lesion tissue is thresholded and cleaned up (by removing cluster smaller than $8mm^3$).

The thresholded posterior probability map for the lesion tissue was compared to the provided lesion mask. The USwL lead to more biologically plausible lesion volumes ($p<.05$), in term of volume compactness [10], see Fig. 3.

The similarity of the warped posterior GM maps across the 20 subjects (expressed as the root-mean square difference to the mean of the 20 subjects) was also examined. The improvement in the between-subject GM-matching, from using CFM-US versus USwL, is proportional ($p<.05$) to the actual WM lesion volume.

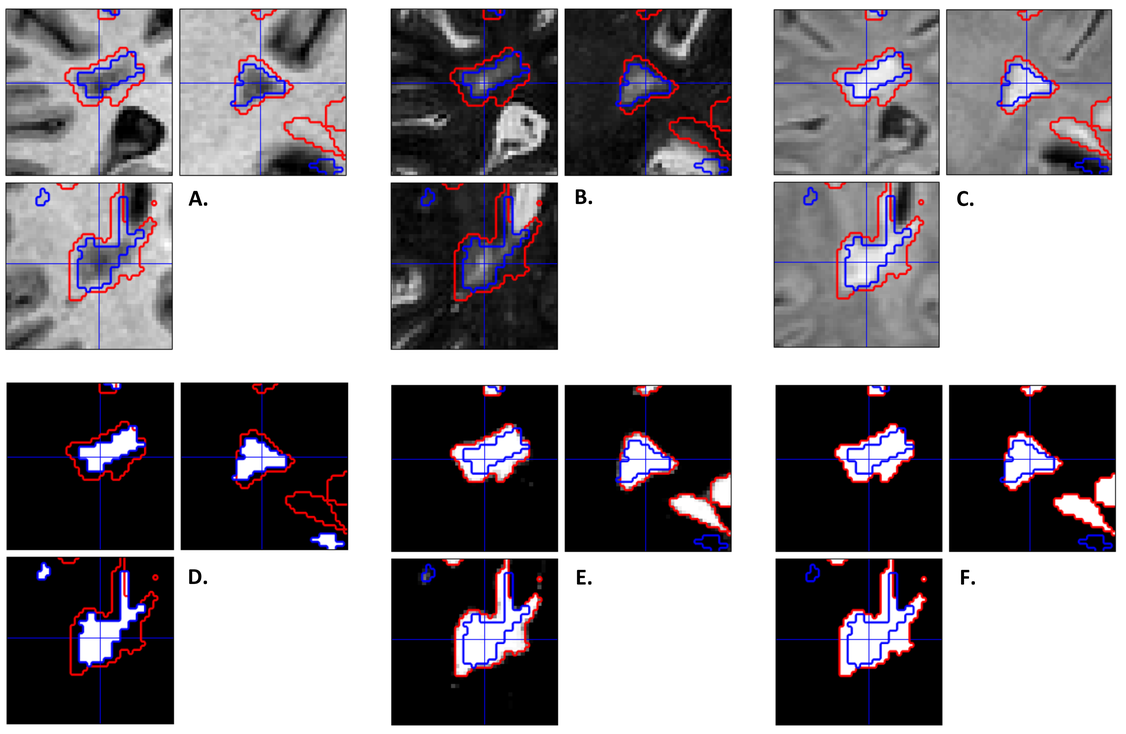

Fig. 3. Illustration of USwL applied on a single MS patient images from the Mschal dataset, where we have (A, B, C) the T1, T2 and FLAIR-weighted structural MR images (resolution is $1x1x1\ mm^3$); (D) manually generated lesion mask provided with its contour displayed in blue over all the images; (E) posterior probability map of the lesion; and (F) thresholded posterior probability map of the lesion (including light clean up of small clusters), with its contour displayed in red over all the images.

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