

Spatial Modeling of Multiple Sclerosis for Disease Subtype Prediction

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Introduction

Multiple Sclerosis (MS) is a chronic inflammatory-demyelinating disease of the central nervous system. MS is divided into five distinct clinical categories (RLRM, PRP, SCP, PRL and CIS) and disease progression differs significantly. In the assessment of MS MRI data is to a large extent only used in a qualitative way, to assess the dissemination of lesions in space and time [6]. Studies have shown that conventional MRI measures (e.g. total lesion volume) have rather low predictive value and are therefore poor indicators for determining clinical outcomes in MS [5].

We compare three different advanced predictive modeling approaches for the 5-way prediction problem; two based on Bayesian spatial modeling and one on SVM.

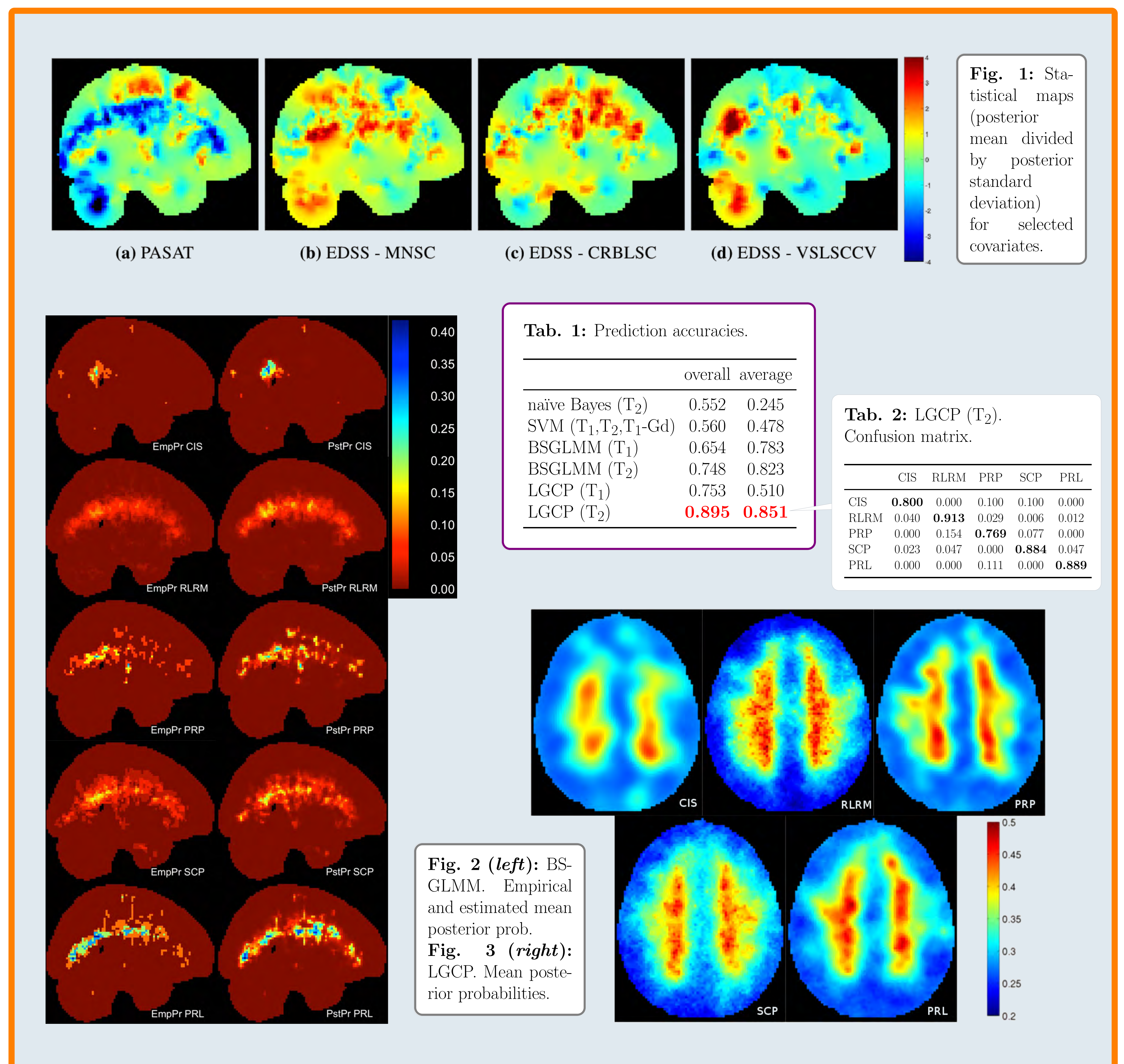
Methods

Bayesian Spatial Generalized Linear Mixed Model (BSGLMM) [3]. Whereas conventional Lesion Probability Mapping fits a General Linear Model at each voxel, this approach respects the binary nature of the lesion data. It comprises a spatially regularized probit regression model and included demographic and clinical covariates.

Bayesian Log Gaussian Cox Process (LGCP). To account for the random location of lesions, this approach converts lesion masks to point valued data, (x,y,z) coordinates of the center of mass of each lesion. The LGCP [7] takes the log of the Poisson intensity function to be the realization of a Gaussian random field; fully characterized by the mean and covariance structure: $\lambda(r) = \exp[m(r) + c(r,r)/2]$, with $c(r,s) = \sigma^2 \exp[-\rho||r-s||^\delta]$.

Both Bayesian methods use MCMC sampling to estimate posterior quantities and an importance sampling technique [4] to estimate leave-one-out predictions.

SVM. Minkowski functionals [1] are used to characterize connectivity and shape of lesions; they correspond to volume, surface area, mean breadth and Euler characteristic. Plus, the (normalized) original images are used to compute ‘texture’ statistics. Summary measures of these geometric and intensity-based characteristics combined with demographic and clinical data are used as feature sets for training of pairwise, non-linear SVM classifiers.



Data. 250 subjects were scanned on a 1.5T scanner at the University Hospital Basel, collecting T_1 , T_2 & T_1 -Gd-enhanced images. Each scan was affine registered to MNI space using trilinear interpolation [2]. Number of subjects per subtype: 11 CIS, 173 RLRM, 13 PRP, 43 SCP, 10 PRL.

Results

Table 1 shows prediction accuracies for all models, revealing the superiority of the spatial approaches. The BSGLMM shows strong prediction results with misclassification predominantly occurring in the CIS subtype. These patients tend to have fewer and smaller lesions than those correctly classified (see Fig. 2).

For T_1 data, the LGCP it performs well on the largest subtype (RLRM) but has difficulty with the smaller groups which might be due to the small number of data points available for these subtypes. For T_2 data, predictions are much more accurate. The LGCP is also the closest to a generative model, i.e. when simulating new data, it would give more realistic predictions than BSGLMM which assumes independent lesion data conditional on (spatially regularized) coefficients.

Conclusions

In contrast to standard methods, the Bayesian spatial models presented here exploit the spatial structure of MS lesion maps and take into account the binary nature of lesion data without an arbitrary smoothing parameter. The BSGLMM is able to provide spatial information, e.g. estimates for the spatially varying effects of EDSS and PASAT (see Fig. 1), which current empirical methods cannot.

The BSGLMM has the interpretability of a traditional regression model but can only account for local spatial dependence; the LGCP doesn't enjoy a regression framework but explicitly accounts for (larger scale) spatial variation in lesion location; and SVM uses a rich constellation of features from all available MRI sequences.

References

- [1] Arns CH, et al. (2001), *Phys Rev E* 63(3): 031112.
- [2] Bendfeldt K, et al. (2009), *NeuroImage* 45: 60–67.
- [3] Ge T, et al. (2014), *Ann Appl Stat* 8(2): 1095–1118.
- [4] Gelfand A, et al. (1992), *Bayes Stat* 4: 147–167.
- [5] Lövblad KO, et al. (2010), *AJNR* 31: 983–989.
- [6] Morgan C, et al. (2010), *Mult Scl* 16: 926–934.
- [7] Møller J, et al. (1998), *Scand J Stat* 25: 451–482.

