Age-Filtered MRS Classifier To Overcome The Differences In Childhood And Adulthood Brain Tumours

J. Vicente[1], J. M. García-Gómez[1], S. Tortajada[1], E. Fuster-Garcia[1], A. Capdevila[2], A. C. Peet[3], B. Celda[4], and M. Robles[1]

[1]IBIME-ITACA, Universidad Politécnica de Valencia, Valencia, Spain, [2]Hospital Sant Joan de Déu, Barcelona, Spain, [3]Birmingham Children's Hospital NHS Foundation Trust, University of Birmingham, Birmingham, United Kingdom, [4]Departamento de Química Física, Universidad de Valencia, Valencia, Spain

Introduction – Pattern recognition applied to in-vivo ^{1}H MRS is becoming an important tool for additional accurate non-invasive technique for classification and characterization of adult Brain Tumours (BT) [1]. Although limited studies have been reported in children, they confirm that childhood BT differ from those arising in adulthood in their relative incidences, histological features, sites of origin and responsiveness to therapy [2].
Purpose – To study the compatibility and improve the design of automatic classifiers for children BT based on MRS. Evaluation of classifiers with two independent test sets of children and adult patients affected by BT. Design of a filter based on the patient age to internally decide when the classifier specialized with child patients should be used.

Materials – 489 (93 children, 396 adults) SV ^{1}H-MRS at 1.5T (TE/TR 20-32/1600-2020 ms) histopathologically diagnosed brain tumor cases acquired by ten institutions in the framework of the INTERPRET and eTUMOUR projects [3,4] has been used for this study. Signal processing was performed following the protocols defined in [5]. Pathology distribution in children was: 60 glials (12 high grade (HG) and 48 low grade (LG)), 24 Medulloblastoma (MED), 3 Meningioma (MEN) and 6 cases belonging to less frequent tumour types (OTH). Distribution of pathology in adults was: 233 glials (156 HG, 77 LG), 2 MED, 69 MEN, 65 Metastasis (MET), 5 Normal brain spectra (NOR) and 22 OTH. Mean age in children and adults was 11.5±8 and 54±13 respectively.

Methods – LDA and KNN children and adult classifiers able to discriminate between aggressive and non-aggressive BT have been developed with a training corpus of 60 children cases and 300 adult cases respectively. Peak integration (PI) to mean metabolites of the region of [0.5,4.1 ppm] interval, Principal Component Analysis (PCA) and PCA applied to the PI were used as different dimensionality reduction techniques to the inputs of the classifiers. An initial evaluation measured with Accuracy (ACC) and the balanced accuracy rate (BAR) estimated on a 10-Folded Cross Validation re-sampling was calculated for each classifier. Children classifiers were tested with two independent test sets: one containing 33 children cases and other with 396 adult cases. Analogously for the adult classifiers, an independent test set of 96 adult cases and a second with the total set of childhood cases (93) were applied. ACC and BAR were calculated for each independent test set applied.

Results – Statistical significant differences were observed between child and adult aggressive BT (Student's T-test, α=0.05 with Bonferroni correction), whilst non-aggressive BT in children and adults did not reflect remarkable differences in metabolite concentration. Figure 1 shows the mean metabolite concentration of aggressive and non-aggressive BT. Mean training performance of adult classifiers was ACC=0.84; BAR=0.84 (see Top Table 1). On the other hand, mean training performance of childhood classifiers was slightly inferior with ACC=0.77; BAR=0.80 (see Bottom Table 1). When applying the adult independent test set to the adult classifiers, similar results to the performance training were obtained. On the contrary, when the children test set was applied to the adult classifiers, a low mean performance was observed (ACC=0.52; BAR=0.50). Analogously, the performance obtained in children classifiers when the childhood independent test set is applied is similar to the training performance although it became significantly worse when the adult test set was applied (mean performance of ACC=0.51; BAR=0.52). The best classifier of each age category was selected and a filter based on the normal probability density of the ages of their respective training cases was applied in order to decide what classifier use for each case to be evaluated. This "filtered classifier" was tested with an independent test set of 33 children cases and 96 adult cases. The performance obtained was similar to the ones obtained by each classifier individually when tested with a test set in accordance to the age of their training samples (ACC=0.84: BAR=0.85; see Table 2).

Table 1 Training and independent test set performances of Adult Classifiers trained with 300 samples and Children Classifiers trained with 60 samples. These classifiers disciminate aggressive and non-aggresive BT. Average performance of the 6 classifiers (PI+LDA; PI+KNN; PCA+KNN; PCA+LDA; PI+PCA+KNN; PI+PCA+LDA) is shown as well as the performance of the best one for each category.

Adults Classifiers	**Training Performance**		**Adults Test Set (96 samples)**		**Children Test Set (93 samples)**	
	ACC	BAR	ACC	BAR	ACC	BAR
Average performance	0.84	0.83	0.78	0.78	0.53	0.50
Best classifier (PI+LDA)	0.85	0.85	0.85	0.85	0.62	0.60
Children Classifiers	**Training Performance**		**Adults Test Set (396 samples)**		**Children Test Set (33 samples)**	
	ACC	BAR	ACC	BAR	ACC	BAR
Average performance	0.77	0.80	0.51	0.52	0.76	0.75
Best classifier (PI+PCA+LDA)	0.84	0.87	0.55	0.50	0.88	0.88

Table 2 Independent test set performance of an age-filtered classifier combination of the best children and adult classifiers. Mixed Test Set of 33 children samples and 96 adults samples.

	Mixed Test Set	
	ACC	BAR
Age Filtered Classifier	0.84	0.85

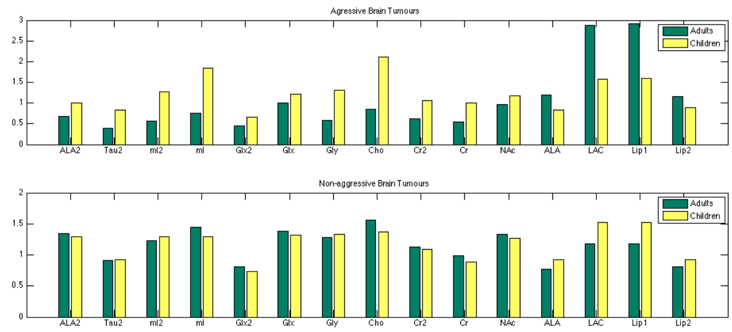

Figure 1 Mean metabolite concentration of aggressive brain tumour (top) and non-aggressive BT (bottom) of adults (green) and children (yellow).

Discussion & Conclusions – Both types of classifiers performed as predicted by their respective training performance when an independent test set of samples with age accordance was applied. On the contrary, when children classifiers were tested with an adult test set and vice-versa (adult classifiers with a children test set), performance lowered drastically. This result reinforces the idea suggested in [2] that the nature of childhood and adulthood BT may be totally different. A simple filter based on the normal probability density function of the age estimated in the training dataset can successfully overcome these differences and obtain a classifier that globally behaves as predicted by the training performance.

Acknowledgements– This work was partially funded by the European Commission (FP6-2002-LIFESCIHEALTH 503094) and (IST-2004-27214). The authors acknowledge to Programa Torres Quevedo from Ministerio de Educación y Ciencia, co-founded by the European Social Fund (PTQ05-02-03386). We thank eTUMOUR and INTERPRET partners for providing data, in particular C. Majós (IDI-Bellvitge), A. Moreno (Centre Diagnostic Pedralbes), Arend Heerschap (RU), J. Griffiths and F. Howe (SGUL), Gajewicz (MUL), Jorge Calvar (FLENI) and J Capellades (IDI-Badalona).

References – [1] NMR Biomed. 2006 Jun;19(4):411-34 [2] CBTR of USA, 2004 Primary brain tumours in United States. [3] INTERPRET: http://azizu.uab.es [4] eTUMOUR: www.etumour.net [5] DOI 10.1007/s10334-008-0146-y.