Quantitative MRI analysis of craniofacial bone marrow in patients with sickle cell disease

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Background: Sickle-cell disease (SCD) patients are chronically deprived of oxygen forcing the body to compensate. It is known that hypoxic states induced by SCD leads to secondary bone marrow changes such as red marrow reconversion and expansion of the marrow space, which can be seen in the craniofacial bones (Ref.1-4). Furthermore, repeated transfusion of packed red blood cells (PRBC) as a form of treatment may lead to increase iron deposition in the marrow.

Purpose: The purpose of this study is to look for specific SCD changes in craniofacial bone marrow by analyzing T1, T2, and secular-T2 relaxation times using quantitative MRI (qMRI). Additionally, we investigated craniofacial bone marrow volumes in SCD patients and compared them to normal subjects.

Materials and Methods: 15 SCD patients (19.8-43 yrs, mean 30.14) and 23 controls (23-59.5 yrs, mean 39.3) were imaged with mixed-TSE pulse sequence at 1.5T (Ref.5,6). The craniofacial bones, not including mandible, were manually segmented on axial 3-mm thick proton density-weighted images using *3D slicer* (http://www.slicer.org/). qMRI algorithms were written in Math CAD 2001i (PTC, Needham, MA). T1, T2, and secular-T2 relaxation time histograms of the bone marrow were modeled with Gaussian functions; peak values were plotted as a function of age. Bone marrow volume was first calculated by segmental volumetry (Figure 2). Volume was then "standardized" to control for random variability of volume by taking the ratio of bone marrow volume to intracranial volume (Ref.7) and plotting as a function of age. Medical records from 2000 through 2009 were analyzed to determine the number of hospitalizations and blood transfusions.

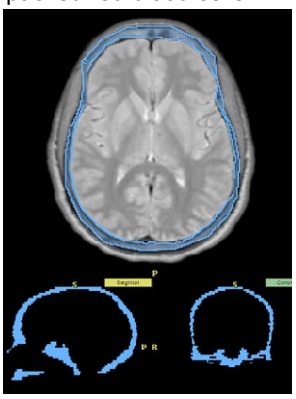

Fig.1: Bone marrow segmentation

Results: Notably, when analyzing T1 histograms, there was a bimodal distribution and a two peak analysis was performed generating two peak values for T1 (Figure 3). The T2 and secular-T2 peak relaxation times were monomodal giving one peak value. Of two T1 peaks, only the first peak (fatty marrow) showed a significant SCD-related increase (499.5 ± 114 ms and 690 ± 100.2 ms p<.0002), although both T1 peaks showed an age-related trend (p<0.005, p<0.002 for T1 peak 1 and T1 peak 2, respectively). T2 and secular-T2 peaks revealed a significant shortening in SCD patients (118.7 ± 11.9 ms and 77.6 ± 20.7 p<.0001; and 130.4 ± 16.3 ms and 81.9 ± 22.9 p<.0001, respectively). Bone marrow volume showed significant increase before and after standardizing to intracranial matter for SCD subjects (432 ± 70.5 $cm^3$and 501.5 ± 67.3 cm^3, p<.008 and 0.33 ± 0.06 and 0.39 ± 0.06, p<.002). Additionally, there was an association between the number of PRBC and T2 times. The correlation coefficient (r) = -0.61 p< .045 for T2 an (r) = 0.60 and p<0.51 for secular-T2 times.

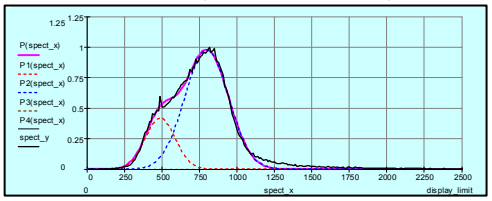

Fig.2: Histogram analysis of T1 peaks in a SCD patient. Bimodal T1 peak distribution is seen

Conclusion: Patients with SCD exhibited significant changes in the craniofacial bone marrow most likely secondary to red marrow reconversion and iron deposits that can be identified by qMRI relaxometry and volumetry. qMRI relaxometry and volumetry may be used as an non-invasive tool for assessment of disease severity.

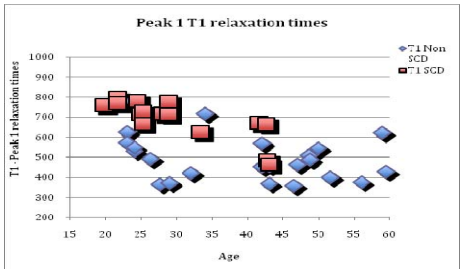

Fig.3: Comparison of peak 1 T1 relaxation times vs. age illustrating significant increase in T1 lengthening in SCD patients compared to controls

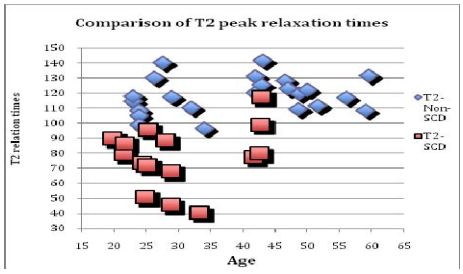

Fig.4: Comparison of T2 peak relaxation times illustrating the significant T2 shortening when comparing SCD patients to controls

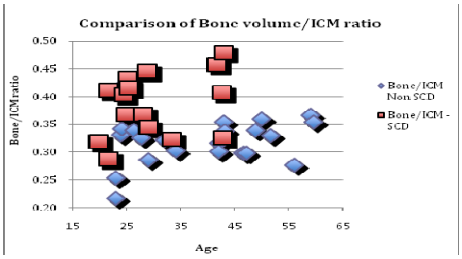

Fig.5: Comparison of bone marrow/ intracranial volume ratio illustrating the significant increase in marrow volume in SCD patients compared to controls

References:

1. Almeida A, Roberts I. **Bone involvement in sickle cell disease.** Br J Haematol 2005; 129(4):482-490.
2. Stamataki S, Behar P, Brodsky L. **Extramedullary hematopoiesis in the maxillary sinus.** Int J Pediatr Otorhinolaryngol 2009; 4:32-35.
3. Lonergan GJ, Cline DB, Abbondanzo SL. **From the archives of the AFIP sickle cell anemia.** RadioGraphics 2001; 21:971-994.
4. Saito N, Banner EN, Nadgir RN, Sakai O. **Sickle cell disease: radiographic manifestations in head and neck.** Proceedings of 94th scientific assembly and annual meeting, Radiological Society of North America, Chicago, November 30-December 5, 2008.
5. Suzuki S, Sakai O, Jara H. **Combined volumetric T1, T2, and secular-T2 quantitative MRI of the brain: age-related global changes (preliminary results).** Magn Reson Imaging 2006; 24(7): 877-887.
6. Saito N, Sakai O, Ozonoff A, Jara H. **Relaxo-volumetric multispectral quantitative magnetic resonance imaging of the brain over the human lifespan: global and regional aging patterns.** Magn Reson Imaging 2009; 27(7):895-906.
7. Blatter DD, Bigler ED, Gale SD, Johnson SC, Anderson CV, Burnett BM, Parker N, Kurth S, Horn SD. **Quantitative volumetric analysis of brain MR: normative database spanning 5 decades of life.** Am J Neuroradiol 1995; 16:241–251.