



Getting the Whole Pediatric Picture with MR Quantification in Under 6 Minutes

For Cincinnati Children's Hospital Center, the now-clinical use of MR quantification proves essential in delivering never-before-seen insights in some of the most challenging pediatric neuro patients.

Summary

To say Cincinnati Children’s Hospital Center is a busy place is quite the understatement. As Southwest Ohio’s only level 1 pediatric trauma center, the facility is home to the country’s busiest pediatric emergency department. And aside from the volume of patients, the 700-bed facility continually is ranked as one of the top children’s hospitals in the country – in 2019, U.S. News & World Report listed it as third among all Honor Roll hospitals.

That’s not an easy task. To ensure even the littlest of patients receive the best care, the facility looks to the leadership of Dr. Leach. Not satisfied with subjective interpretations to MR images, Dr. Leach sought a whole-brain volume quantification solution that delivered multiple image contrasts using one acquisition in a reasonable time. He found it with SyMRI from SyntheticMR.



JAMES LEACH, MD

James (Jim) Leach, MD, is a neuroradiologist specializing in pediatric neuroradiology at Cincinnati Children’s Hospital Medical Center and medical imaging professor at University of Cincinnati Department of Radiology.

Myelin measurements – a clinical first

“When you have a child with an abnormal head size without a known cause, we need to know why,” explains Dr. Jim Leach. “Typically, it’s difficult to get an accurate measurements of cerebrospinal fluid (CSF). We’d have to send the images to a processing environment, which is often difficult for a clinical radiologist to use – and then the results are confusing. We also didn’t have a way to determine if the myelin development was abnormal. Now, we can access the data immediately when we are reading out and have an accurate measurement of whole brain myelin. I don’t have any other clinical means that allows me to do that. It’s a very important development.”

From assumption to quantitative evaluation

Instead the typical neuro MR scans that can lead physicians to make assumptions based on visual interpretation, Dr. Leach and his team use SyMRI for a quantitative evaluation. “It helps us make decisions about what’s normal and what’s not,” explains Leach. “Now, we can monitor the development and production of myelin as well as white and grey matter in a quantitative environment in minutes – meaning better diagnostic certainty. And when you’re dealing with kids, leaving anything to question isn’t acceptable.”



5–6 minutes in the scanner



Post-processing time in less than 10 seconds



More than 8 pre-set contrast-weighted images

Expanding the Diagnosis

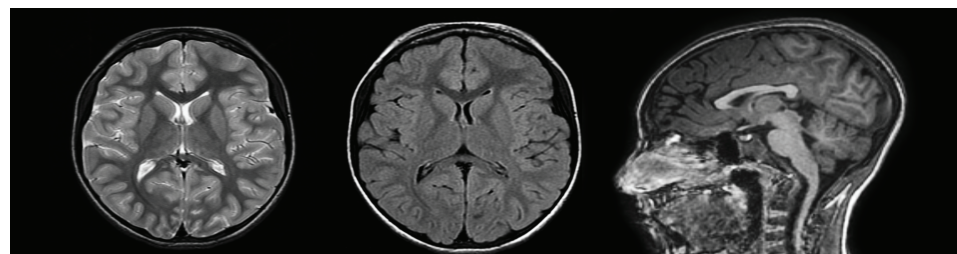
AKT3 DELETION

An extremely rare occurrence, AKT3 microdeletions in 1q45-q4 can have significant effects on brain and head size. The AKT3 protein belongs to the protein kinase B (PKB/Akt) family, which is involved in cell survival, proliferation, and growth.

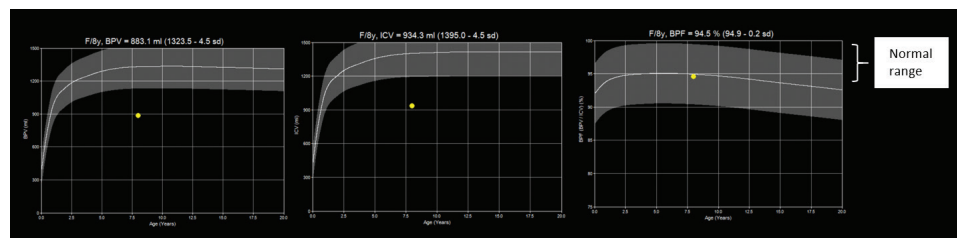
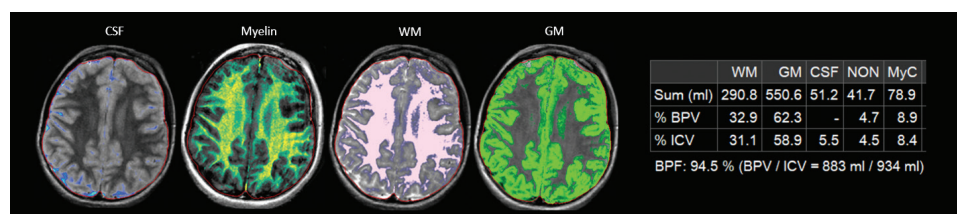
MRI findings in patients with AKT3 microdeletions include microcephaly and corpus callosum agenesis. Phenotypes vary on size and location of deletion, and most have microcephaly. The brain, however, is normal otherwise.

Case #1

Eight-year-old female presenting with developmental delay.



Initial MR assessment of the brain revealed no abnormalities.



KEY: BPF: Brain Parenchal Fraction CSF: Cerebral Spinal Fluid ICV: Intracranial Volume
BPV: Brain Parenchymal Volume GM: Grey Matter WM: White Matter

Subsequent SyMRI sequence performed, providing both scans and comparisons with normal patient population.

Scan shows ICV as very low for her age, as well as BPV. BPF (the percentage of intracranial volume taken up by the brain) was in the normal range, consistent with abnormal brain growth rather than volume loss.

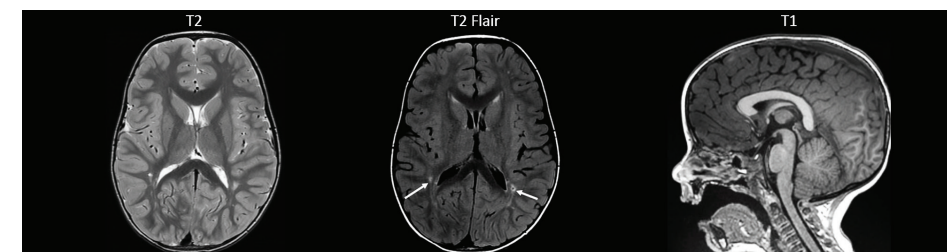
As expected, both white matter and grey matter volume were decreased, as well as total myelin volume. Myelin fraction (percentage of BPV that is myelin) was in normal range, indicating that this is simply because of the small brain, rather than poor myelination. CSF volume is normal.

Overall findings are compatible with a primary abnormality of brain growth, suggesting a genetic cause.

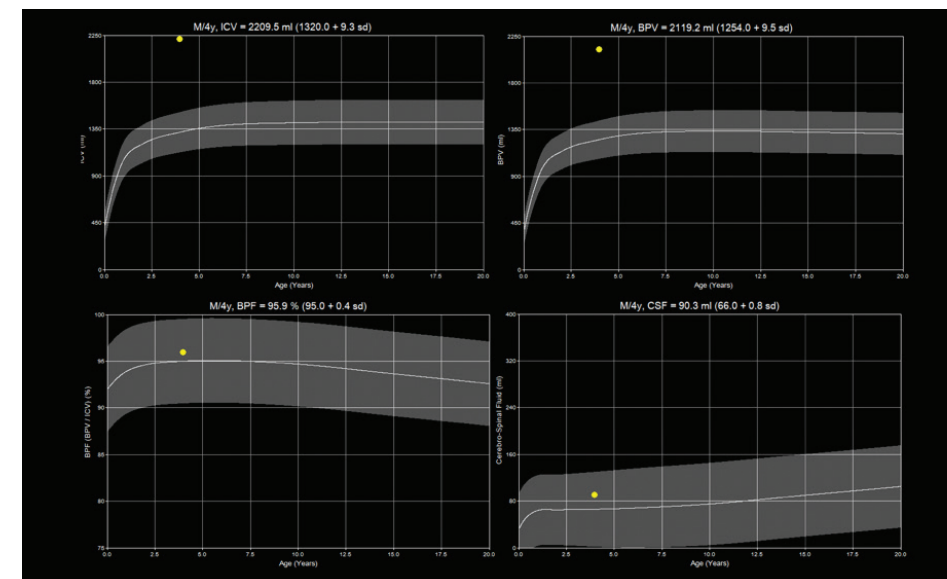
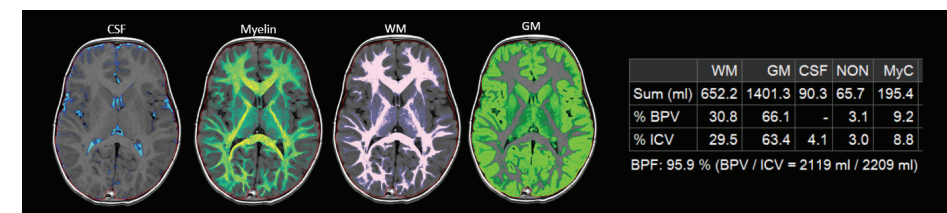
Prognosis: Subsequent genetic testing revealed an AKT3 deletion, a known abnormality resulting in decreased brain growth and microcephaly.

Case #2

Four-year-old male presenting with developmental delay in language skills and enlarged head circumference.



Visual inspection of MR scan revealed only minimal increase in signal in the deep white matter of both parietal lobes.



KEY: BPF: Brain Parenchal Fraction CSF: Cerebral Spinal Fluid ICV: Intracranial Volume
BPV: Brain Parenchymal Volume GM: Grey Matter WM: White Matter

As expected, both white and grey matter volumes are increased for age, as well as myelin volume while CSF is in normal range. ICV and BPV markedly elevated for patient's age; normal BPF. The markedly enlarged brain size with minimal increase in white matter signal while non-specific, suggests a genetic cause, possibly PTEN mutation.

Prognosis: Genetic testing confirmed PTEN mutation. Patient diagnosed with Cowden syndrome.

Expanding the Diagnosis

ENLARGED BRAIN

PTEN hamartoma tumor syndrome (PHTS) refers to a group of clinical syndroms of aberrant growth due to germline mutations in the PTEN tumor suppressor gene. Cowden syndrome, which was the final diagnosis of this patient, is the most common phenotype (80%).

Neuroimaging in PTEN-positive patients demonstrates either enlarged perivascular spaces, multifocal periventricular white abnormalities, or both. In evaluating MRI patterns in patients with macrocephaly (>2 SD above the mean) and developmental delay and/or autistic behaviors, PHTS should be considered.

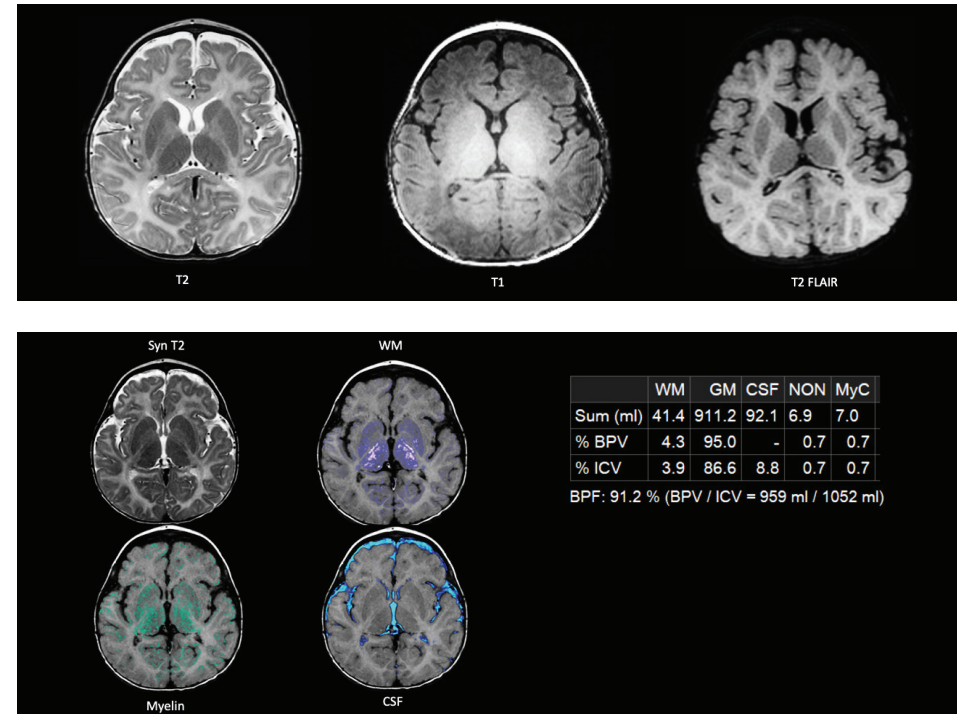
This case demonstrates that it's feasible to identify actual enlargement of the brain in this condition.

Findings

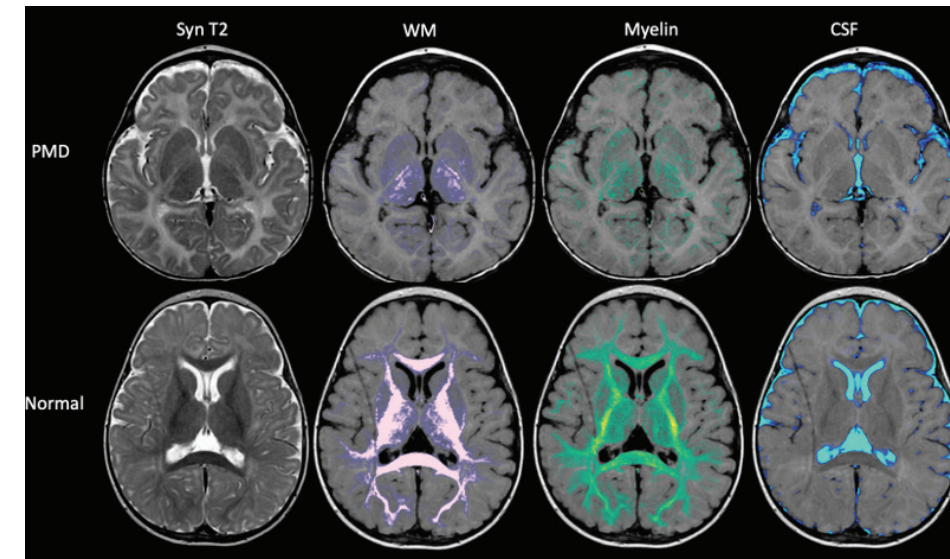
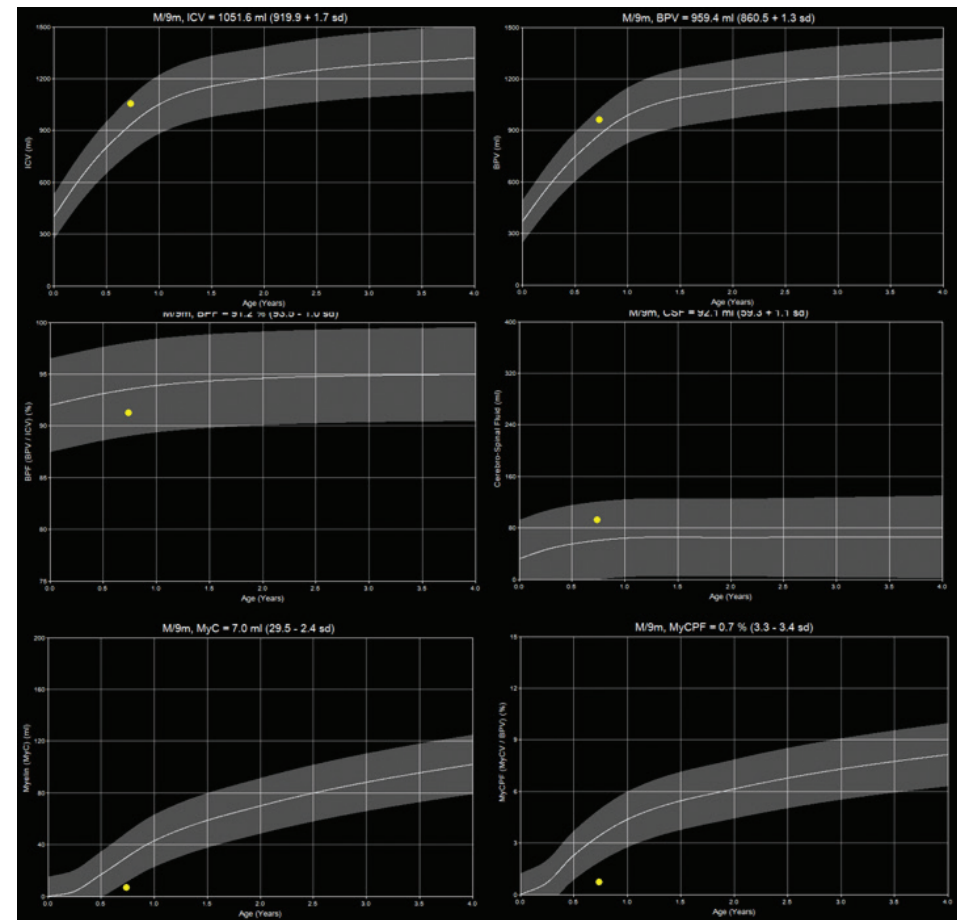
SyMRI indicates that although ICV, BPV, and BPF are normal, white matter volume is decreased, with normal grey matter volume and CSF. There is noticeable decrease in myelin volume for patient's age. Overall findings are compatible with a primary myelination disorder, and when combined with clinical history, is most consistent with Pelizaeus-Merzbacher disease.

Case #3

Eight-month-old male presenting with nystagmus and gross motor delays.



MR examination showed little myelination without other gross abnormality.



Comparative scans of patient and normal eight-month-old child. Note the dramatic differences in white matter and myelin. In this case, there is almost no visible myelin.

Prognosis: Genetic work-up revealed the pathogenic variant (p.Ala247Thr), PLP1 diagnostic of PMD.

Expanding the Diagnosis

MYELIN QUANTIFICATION

Disorders of myelination have traditionally been more difficult to diagnose, particularly for the inexperienced reader of pediatric neuroimaging. The ability to quickly quantify myelin is a significant improvement over common practices, and can mean significant improvements in diagnosis accuracy for difficult cases like Pelizaeus-Merzbacher disease (PMD).

While signs of PMD vary widely, patients generally present with a marked developmental delay, nystagmus, and increasing weakness as the patient ages.

For the radiologist, PMD appears as a low-signal intensity white matter on a CT scan. On MRI, however, it appears as lack of myelination, as opposed to myelin destruction. Severe cases can show a complete absence of low T2 signal intensity within the white matter. The cerebellum may also be atrophic.

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About SyMRI

SyMRI, which is FDA cleared for patients of all ages, combines an MR sequence with post-processing MR software, and includes multiple contrast-weighted images, fully adjustable for TE, TR, and T1 values for optimal flexibility. This enables automatic segmentations and volume measurements of tissue such as white matter, gray matter, cerebrospinal fluid, and myelin to allow users to track disease progression or compare against control groups. Using a single 6-minute scan with a post-processing time of less than 10 seconds, SyMRI is available both as a stand-alone solution or be fully integrated into the clinical workflow.

About Cincinnatti Children's

As a non-profit academic medical center that was established in 1883, Cincinnatti Children's is one of the oldest and most distinguished pediatric hospitals in the U.S. earning the ranking of 3 in the 2019-20 U.S. News & World Report survey of best children's hospitals. With more than 600 registered beds, Cincinnatti Children's had more than 1.3 million patient encounters and served patients from all 50 states and 58 countries, including 589 international patients in 2017.



SyntheticMR AB develops and markets innovative software solutions for Magnetic Resonance Imaging (MRI). SyntheticMR AB has developed SyMRI®, delivering multiple, adjustable contrast images and quantitative data from one 5-6 minutes scan. The SyMRI product is available in different packages. SyMRI IMAGE provides fast MRI workflows, allowing high patient throughput. SyMRI NEURO enables automatic segmentation of brain tissue, providing objective decision support. SyMRI Research Edition includes exportable SyMaps™, parametric T1, T2 and PD maps of the brain, allowing the investigation to be taken even further. SyMRI is a CE-marked and FDA 510(k) cleared product. SyMRI is a registered trademark in Europe and in the USA. SyntheticMR is listed on the Spotlight Stock Market exchange in Stockholm, Sweden.