DIFFUSION TENSOR IMAGING (DTI) CORRELATES WITH TRANSCRANIAL MAGNETIC STIMULATION (TMS) FINDINGS IN EARLY ALS (AMYOTROPHIC LATERAL SCLEROSIS) DIAGNOSTIC

A. Roceanu[1], V. Ferastraoaru[1,2], M. Onu[3], E. Tarta[4], T. Lupescu[5], O. Bajenaru[1]

[1]Neurology Department, University Emergency Hospital of Bucharest
[2]Jacobi Medical Center, Bronx NY, USA
[3]Radiology Department, "Prof. Dr. Th. Burghele" Hospital
[4]Anatomy Department, University of Medicine and Pharmacy "Carol Davila"
[5]Neurology Department, "Agripa Ionescu" Hospital

ABSTRACT

The onset of ALS is insidious and symptoms may be disregarded by the patient for several months. The diagnosis of ALS is based on clinical features and EMG findings.
DTI offers the advantage of the revealing in vivo macroscopic geometrical arrangement of white matter bundles that becomes apparent through diffusion measurements of water molecules. DTI findings could correlate with prolonged cortical MEP, sustaining the early diagnosis of ALS, revealing upper motor neurons involvement.

Key words: ALS (amyotrophic lateral sclerosis), DTI (diffusion tensor imaging), transcranial magnetic stimulation (TMS)

Background

ALS (amyotrophic lateral sclerosis) is characterised by degeneration of the upper motor neurons (UMN) (cortical motor neurons) and of the lower motor neurons (LMN) (in the cranial nerves nuclei, spinal cord).

The onset of (ALS) is insidious and symptoms may be disregarded by the patient for several months.

The diagnosis of ALS is based on clinical features and EMG findings.

The revised El Escorial Criteria (EEC) is the gold standard of ALS diagnosis.

Recently Awaji Criteria – consider the fasciculation potentials as sign of active denervation (even in the absence of fibrillation potentials and positive waves) in a typical clinical ALS picture; they have higher sensitivity than EEC, without increasing the rate of false positive diagnoses (de Carvalho, 2008). Signs of denervation on EMG could be regarded as equivalent of LMN signs (1, 2).

Also, according to Awaji Criteria, transcranial magnetic stimulation (TMS) findings – changes of the central conduction time and of the motor evoked potentials (MEP) size – may reveal UMN involvement. Cerebral MRI is necessary in order to rule out other disorders. New neuroimaging techniques based on MRI as DTI (diffusion tensor imaging) could be useful in early revealing UMN involvement – in order to obtain surrogate markers for disease progression.

DTI is used for quantification of water diffusion in tissues. DTI offer unique information on white matter and 3D visualization of neuronal pathway.

Water molecules' motion or diffusion was found to be much faster along the white matter fibers than

Author for correspondence:
Adina Roceanu, MD, Emergency University Hospital, 169 Splaiul Independentei, District 5, Zip Code 7050098, Bucharest, Romania
e-mail: adinaroc@hotmail.com

perpendicular to them (Basser et al., 1994). The difference between these two motions (parallel and perpendicular to the fibers, also termed diffusion anisotropy) is the basis of DTI.

DTI takes advantage of the macroscopic geometrical arrangement of white matter bundles that becomes apparent through diffusion MRI measurements.

DTI assess diffusion using **parameters**:

- **FA** (fractional anisotropy) – measures the degree of the preference for a single direction of diffusion.
- **ADC** (apparent diffusion coefficient) – estimates total diffusion for each voxel analyzed and will increase if biological tissues are affected (no diffusion hinders).

Lambda 1, **2** or **3 (F 1, 2, 3)** reviews magnitude of diffusion along most preferred direction (1) to least favored diffusion (space) direction (3).

Pajevic and Pierpaoli suggested color-coded schemes to visualize this 3D information in two dimensions. The most basic red-green-blue (RGB) color-coded scheme attributes a color for each orientation of the fibers: fibers crossing from left to right are visualized in red, fibers crossing anteriorly-posteriorly are visualized in green, and fibers crossing inferiorly-superiorly are visualized in blue. (3,4)

Since the introduction of this methodology in 1994 (Basser et al.) it has been used to study the white matter architecture and integrity of the normal and diseased brains (multiple sclerosis, stroke, aging, dementia, schizophrenia, etc.).

Advanced neuroimaging applications to patients suffering from ALS and other motor neuron disorders (MND) have a high potential in terms of understanding the pathophysiology and visualizing the in vivo pathoanatomy of the diseases.

For the analysis of the white matter integrity with respect to tissue diffusivity and white matter connectivity including fibre tracking algorithms, diffusion tensor imaging (DTI) which can also be performed on a whole brain-basis is of the highest potential to date. Especially both the degree of damage to motor areas and the involvement of non-motor areas are of interest to be subjected to quantitative assessment, in order to establish quantitative surrogate markers for disease progression. (5)

CASE PRESENTATION

We report a 65 years old male, who has a distal weakness in the distal part of the right upper limb, with a progressive onset for about 1 year. Family history was unremarkable.

Clinical examination disclosed upper motor neuron signs (generalised hyperreflexia, left Babinski sign) and also lower motor neuron signs (weakness, atrophy of right hand muscles, inconstant – fasciculation of the tongue), in the absence of sensory signs.

Several investigations were performed:

Biological tests were irrelevant.

Neurogenic changes in EMG (fibrillations, fasciculations in more regions), normal motor, sensory conduction velocities, and the absence of conduction block favours ALS diagnosis.

Cervical MRI revealed a cervical spondylosis – but we considered it as co-morbidity because of the widespread changes in EMG, of the prolonged MEP (motor evoked potentials) elicited from the cortex.

Cerebral MRI showed atrophy of motor cortices. DTI (diffusion tensor imaging) technique was applied in order to demonstrate wallerian degeneration of the cortico-spinal tract.

CONCLUSION

DTI offers the advantage of the revealing in vivo macroscopic geometrical arrangement of white matter bundles that becomes apparent through diffusion measurements of water molecules. In our case, DTI findings correlate with prolonged cortical MEP, sustaining the early diagnosis of ALS.

An early ALS diagnosis is difficult, alternative diagnosis should be ruled out. Medication with riluzole (glutamate-release antagonist) – should be initiated as early as possible, because the neuroprotective effect is greater when medication is started earlier (Bromberg, 1999).

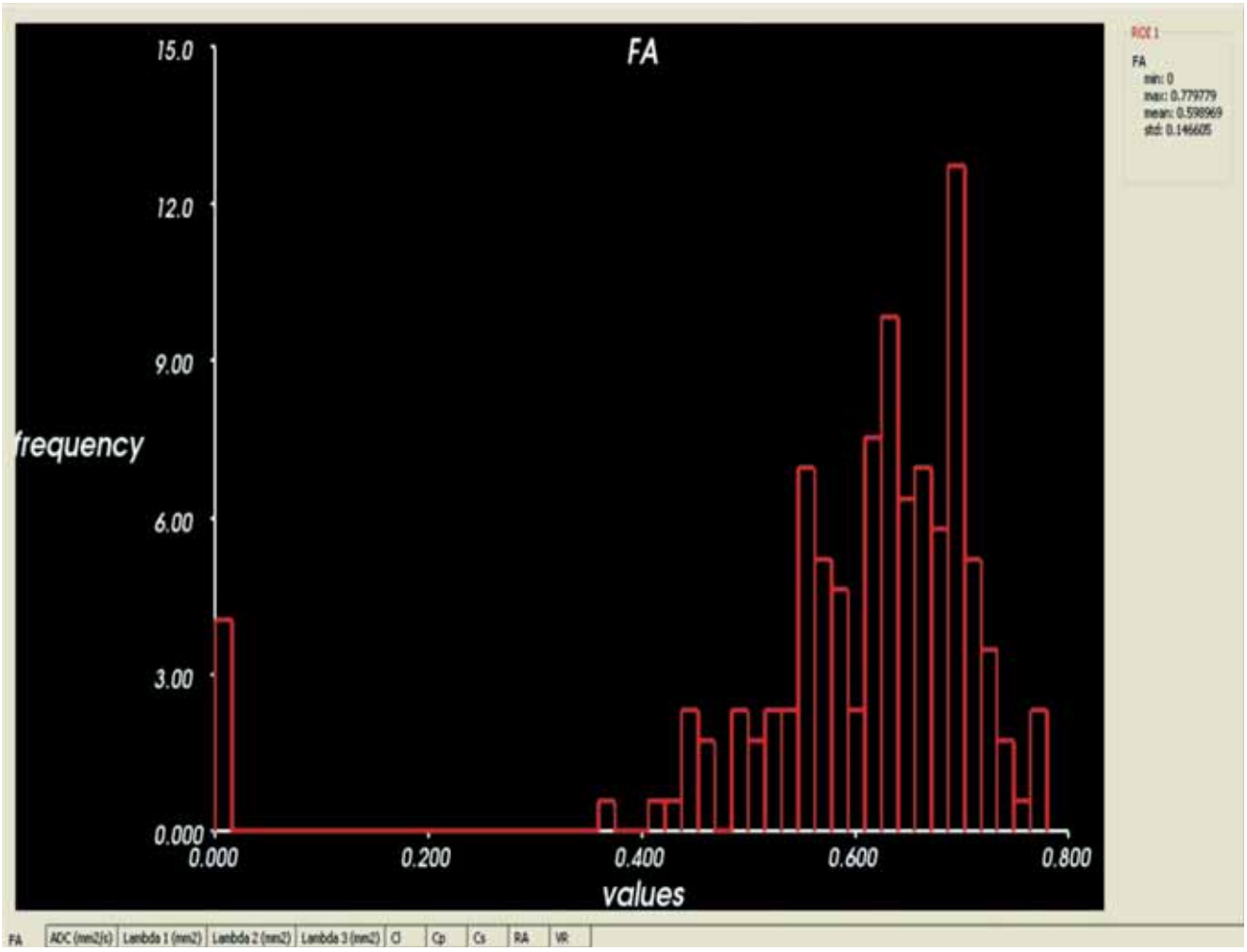

Figure 1a. *FA (fractional anisotropy) – pyramidal tract*

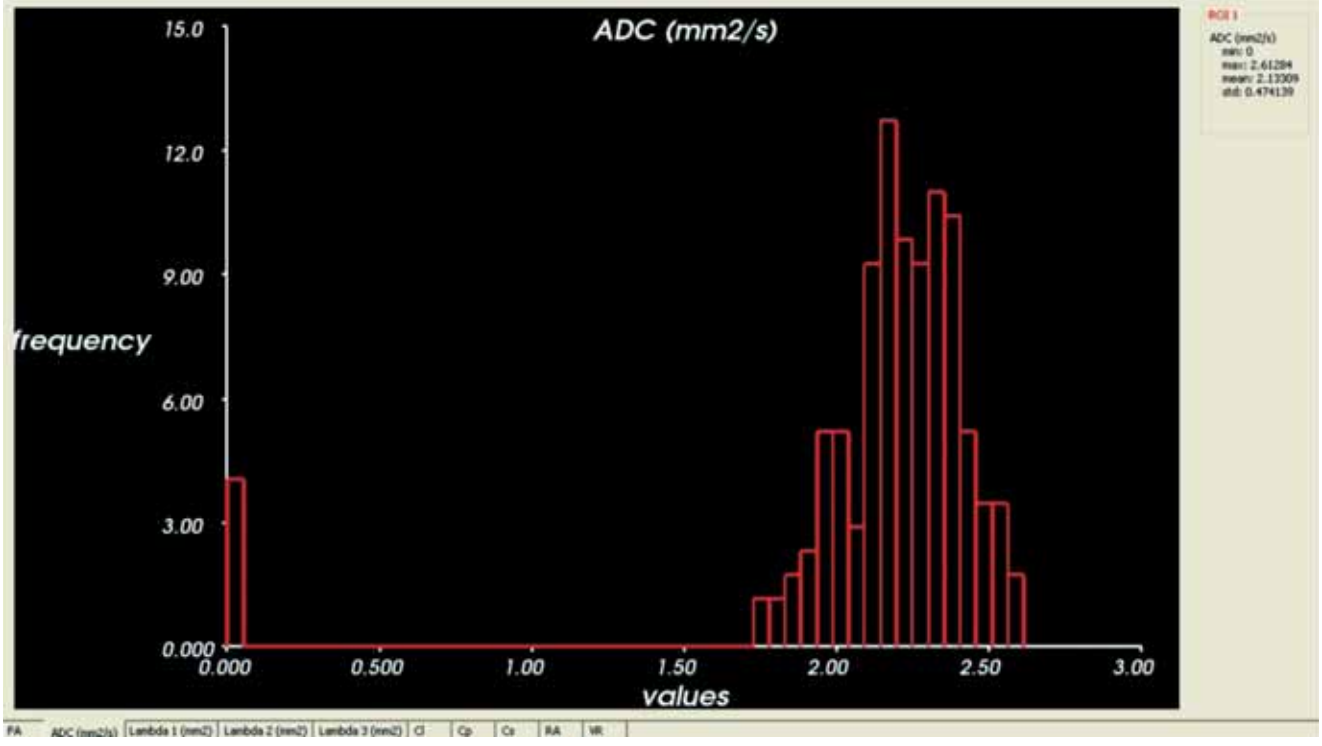

Figure 1b. *ADC (apparent diffusion coefficient) – pyramidal tract*

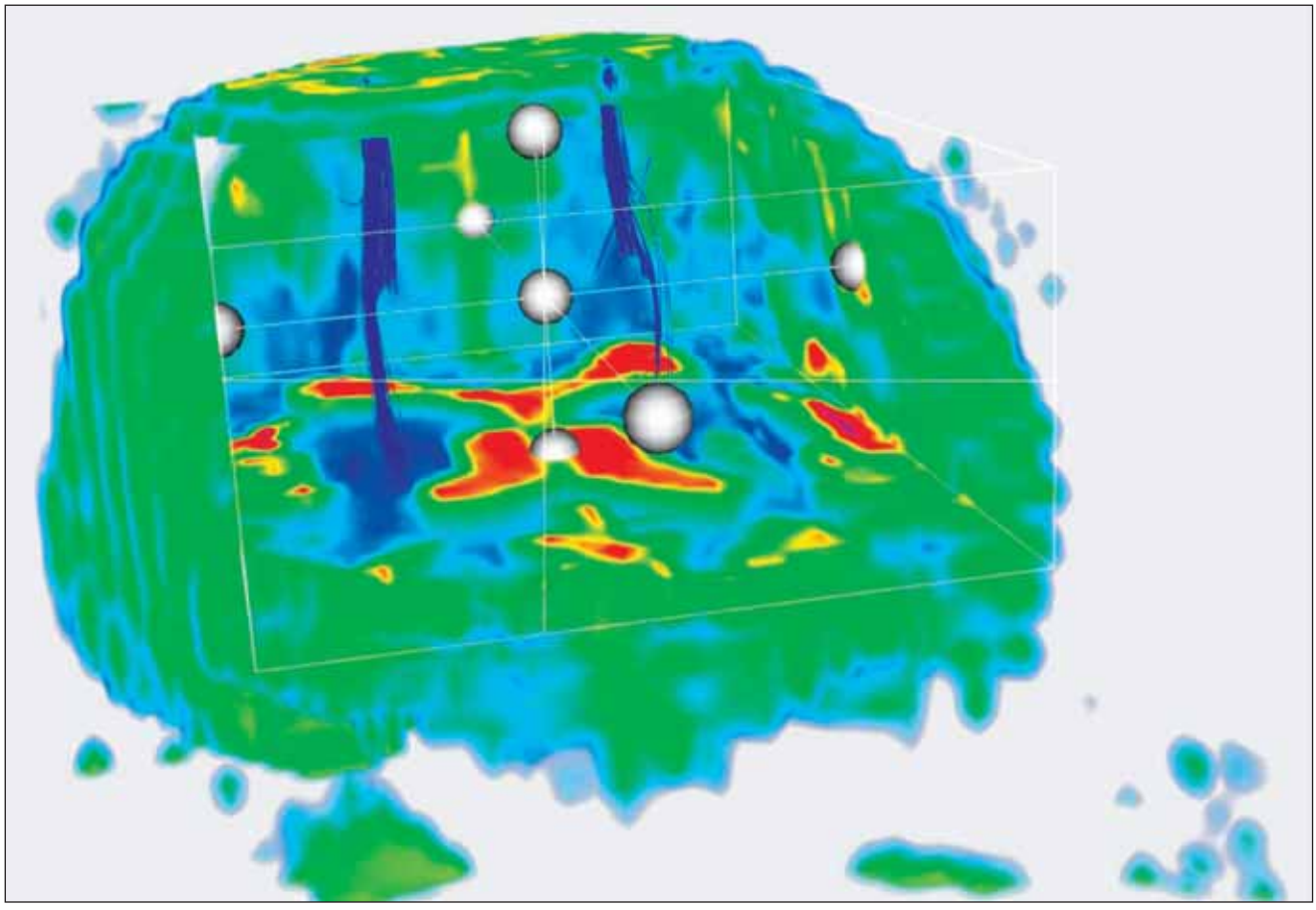

Figure 2a. *FA (fractional anisotropy) – pyramidal tract*

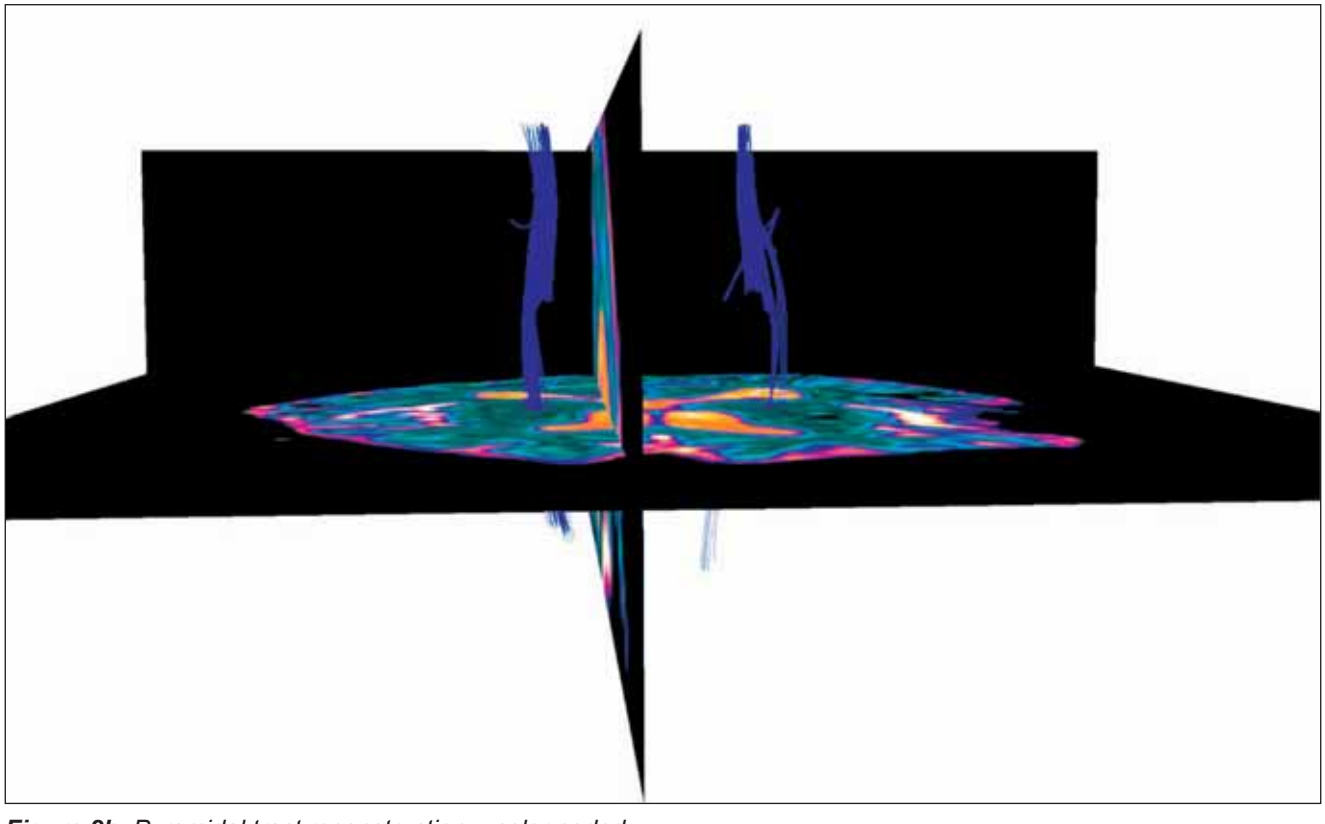

Figure 2b. *Pyramidal tract reconstruction – color-coded*

REFERENCES

1. **Dengler R.** – „Diagnostic criteria of amyotrophic lateral sclerosis (ALS)", *Romanian Journal of Neurology*, Volume IX, No. 4, 2010
2. **De Carvalho M., Dengler R., Brannagan T. 3rd et al** – „Electrodiagnostic criteria for diagnosis of ALS", *Clin Neurophysiol* 2008; 119:497-503
3. **Basser P.J., Jones D.K.**- „Diffusion-tensor MRI: theory, experimental design and data analysis – a technical review". *NMR Biomed* 2002; 15:456-467
4. **Pierpaoli C., Jezzard P., Basser P.J. et al** – „Diffusion tensor MR imaging of the human brain", *Radiology* 1996; 201:637-648
5. **Grosskreutz J., Peschel T., Unrath A. et al** – „Whole brain-based computerisez neuroimaging in ALS and other motor neuron disorders", *Amyotroph Lateral Scler* 2008 Aug; 9(4):238-248
6. **A. Roceanu, V. Ferăstrăoaru, O. Băjenaru et al** – Tehnica DTI (Diffusion Tensor Imaging)", medicalUPDATE, mai 2010; p. 160-164
7. **V. Ferastraoaru, A. Roceanu, O. Băjenaru et al** – "Tractography and parameters analysis methods for cerebral fibers using Diffusion Tensor Imaging", The 7th Congress of Romanian Society of Neurology, *Romanian Journal of Neurology*, Volume VII, Suppl. 1, 2009; p. 27
8. **A. Roceanu, V. Ferastraoaru, O. Băjenaru et al** – "Diffusion Tensor Imaging (DTI) use in early diagnosis of ALS (Amyotrophic Lateral sclerosis) – case presentation", The 7th Congress of Romanian Society of Neurology, *Romanian Journal of Neurology,* Volume VII, Suppl. 1, 2009; p. 31
9. **Bromberg M.** – „Accelerating the diagnosis of amyotrophic lateral sclerosis", *The Neurologist* 1999; 5:63-74