UNIVERSITÀ DEGLI STUDI
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Esperto per la
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A PET/CT approach to spinal cord metabolism in amyotrophic lateral sclerosis

Cecilia Marini, Angelina Cistaro, Cristina Campi, Andrea Calvo, Claudia Caponnetto Flavio Mariano Nobili, Piercarlo Fania, Mauro C. Beltrametti, Cristina Moglia, Giovanni Novi, Ambra Buschiazzo, Annalisa Perasso, Antonio Canosa, Corrado Cabona, Carlo Scialò, Elena Pomposelli, Anna Maria Massone, Maria Caludia Bagnara, Stefania Cammarosano, Paolo Bruzzi, Silvia Morbelli, Gianmario Sambuceti,

Gianluigi Mancardi, Michele Piana and Adriano Chiò

Issues in ALS

Lack of “marker(s)” for:

1. Disease diagnosis
2. Disease prognosis
3. Treatment response

Purpose of the study

To develop a **computational method to systematically evaluate spinal cord metabolism** as a tool to monitor disease mechanisms.

Methods

30 spinal-onset ALS patients were enrolled in the study.
Data obtained in the patients were compared with data from
30 control subjects without any history of neurodegenerative disease.

Patients underwent, after **FDG administration**,
a 3D whole-body scan using an integrated **PET/CT scanner.**

Methods

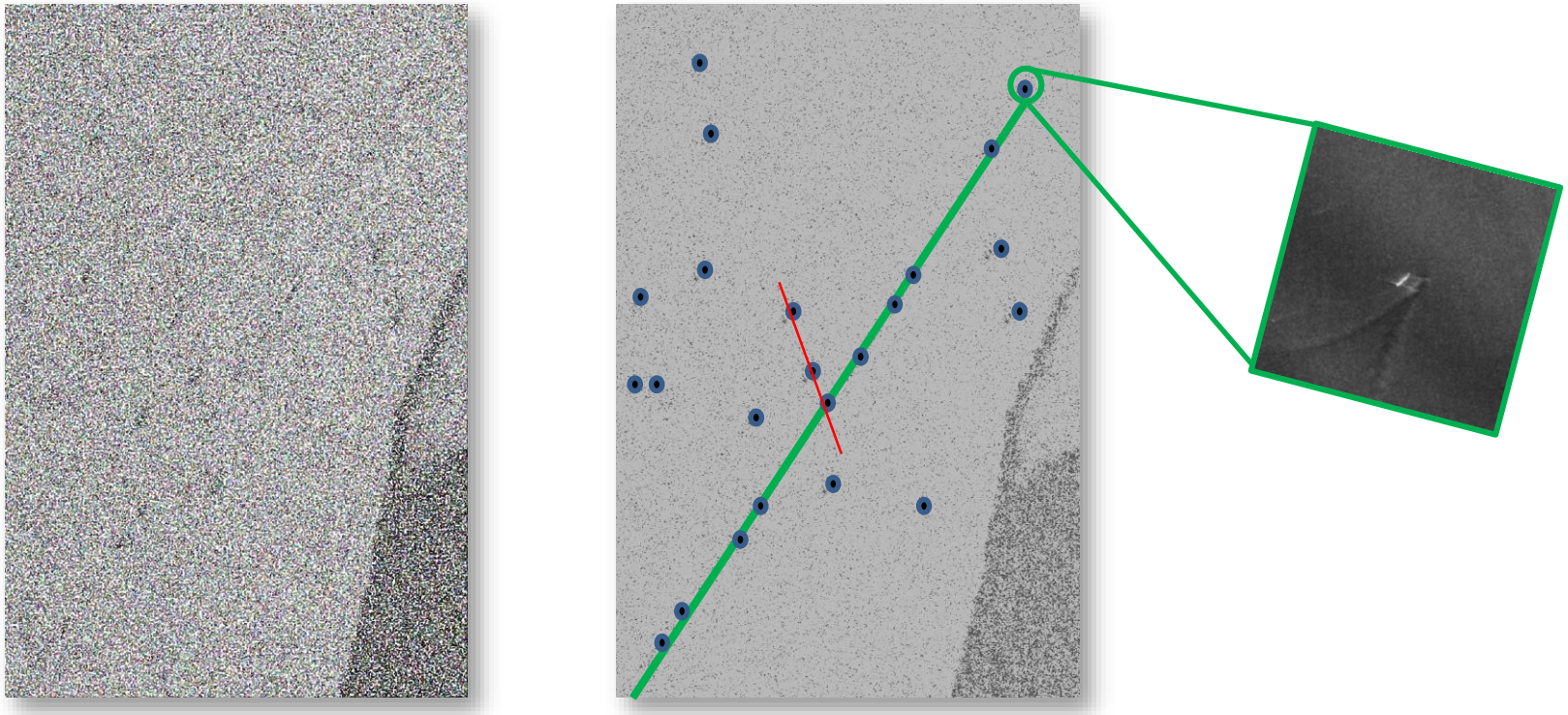
Spinal canal and spinal cord districts were **defined anatomically** considering:

- **Cervical segment:** the region **between the skull base** and the plane adjacent to the **caudal face of the C7** vertebral body.

- **Dorsal segment:** the district **between the caudal face of C7** and the one adjacent **to the caudal face of D12**.

Methods

Hough transform and recognition of lines from satellite pictures.

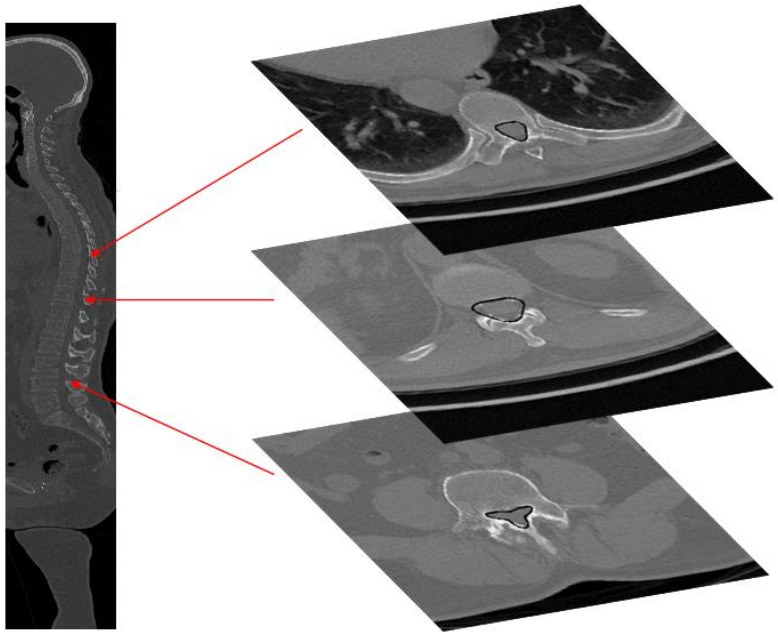


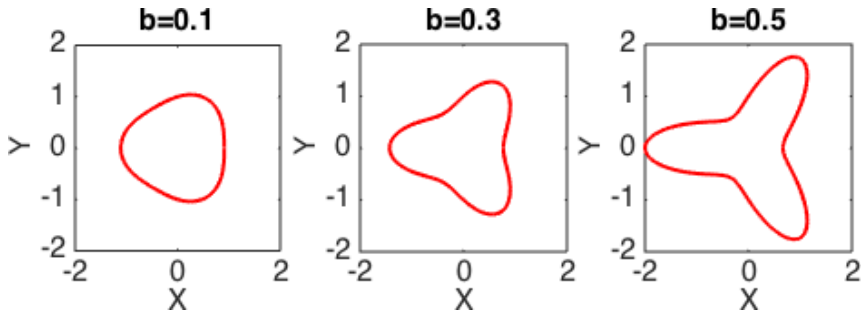
Methods

Masks for each CT slices were then created using Hough transform and:

- **Curves with three convexities** for optimal detection of the **spinal canal**:

$$C_{a,b}: \left(x^2+y^2\right)^3 = \left(a\left(x^2+y^2\right) - b\left(x^3 - 3xy^2\right)\right)^2$$





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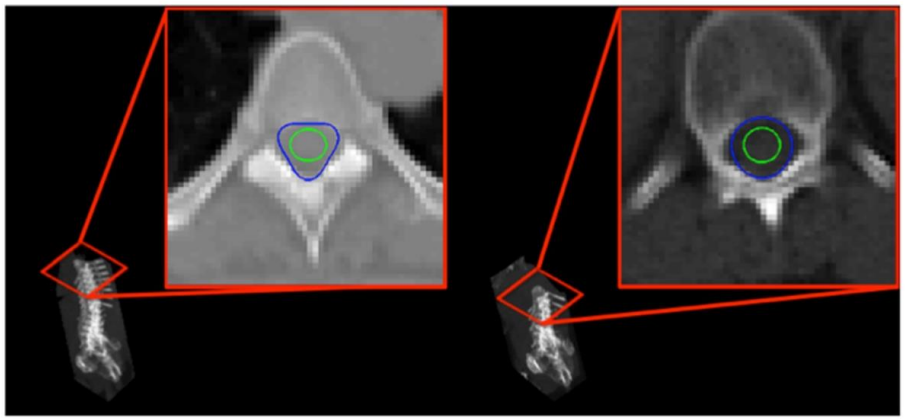
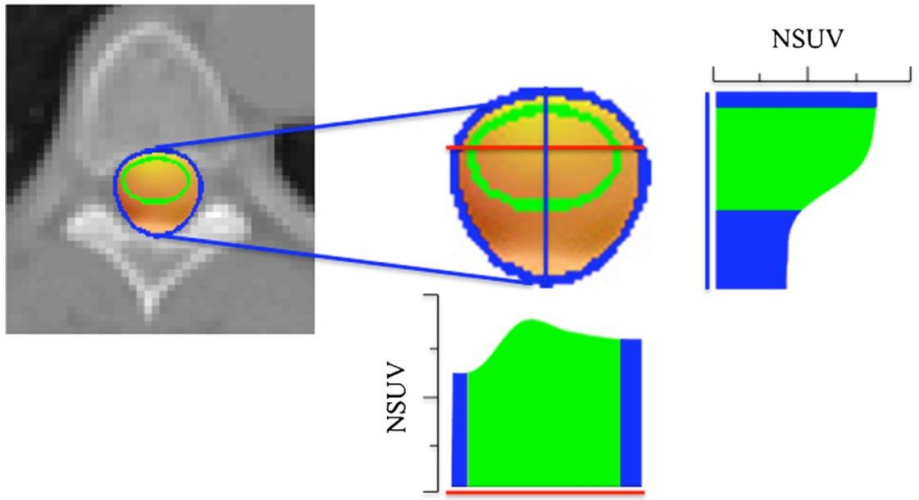
- Four-parameter **ellipses** for identification of the **spinal cord district**:

$$E_{a,b,c,d}: \ b^2(x-c)^2 + a^2(y-d)^2 - a^2b^2 = 0$$



Methods

18F-FDG **standardized uptake values were measured to estimate the metabolic activity** of the spinal canal and cord.



$$SC_NSUV = \frac{(C_NSUV \times cervical\ SC\ volume) + (D_NSUV \times dorsal\ SC\ volume)}{cervical\ SC\ volume + dorsal\ SC\ volume},$$

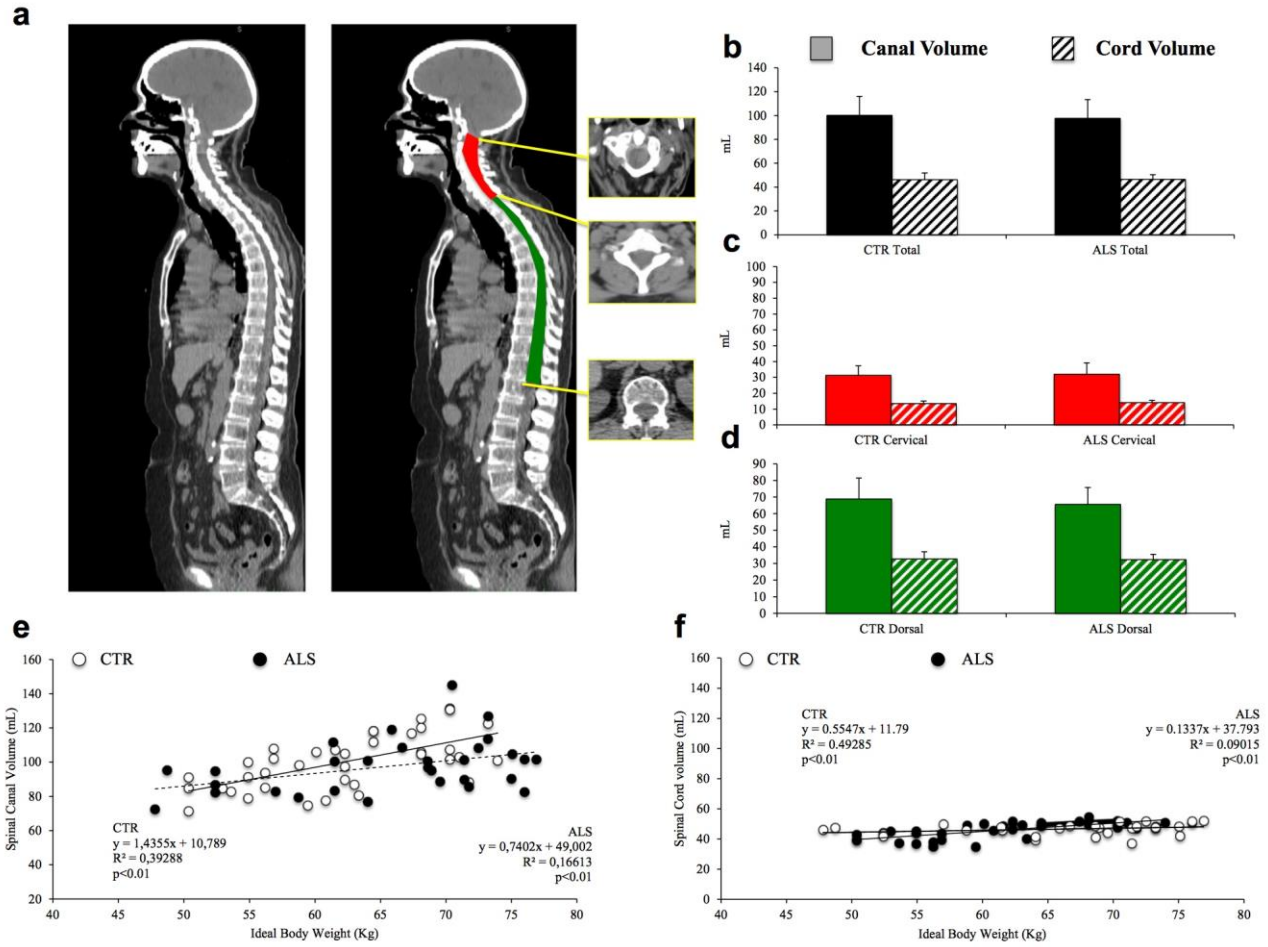
Results (1)

Clinical characteristics of the patients and controls:

Characteristic	Control subjects	ALS patients
Age (years)		
Mean ± SD	60 ± 13	66 ± 11
Median (range)	59 (33 – 79)	69 (34 – 82)
Number of subjects		
Men	20	20
Women	10	10
Ideal body weight (kg), mean ± SD	66 ± 9	66 ± 9
Time from ALS diagnosis to PET/CT (months)		
Mean ± SD	–	18 ± 15
Median (range)	–	17 (2 – 69)
ALS functional rating scale score		
Mean ± SD	–	39 ± 5
Median (range)	–	39 (20 – 46)
Riluzole therapy, *n*	–	21
Serum glucose (mg/dL)		
Mean ± SD	98 ± 13	102 ± 12
Median (range)	100 (73 – 130)	98 (69 – 129)
Follow-up after PET/CT (months)		
Mean ± SD	24	14 ± 7
Median (range)	–	16 (1 – 36)
Number of deaths during follow-up	0	13

Results (2)

Shape and volume of spinal canal and spinal cord:



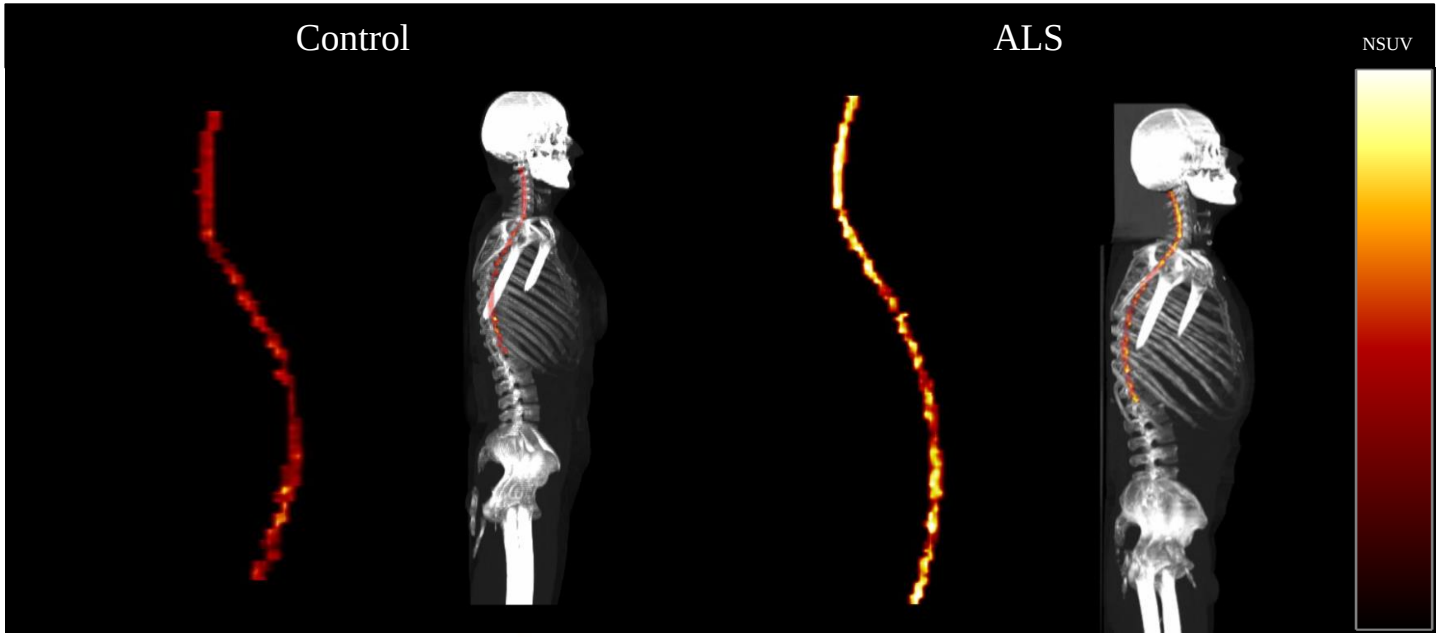
Results (2)

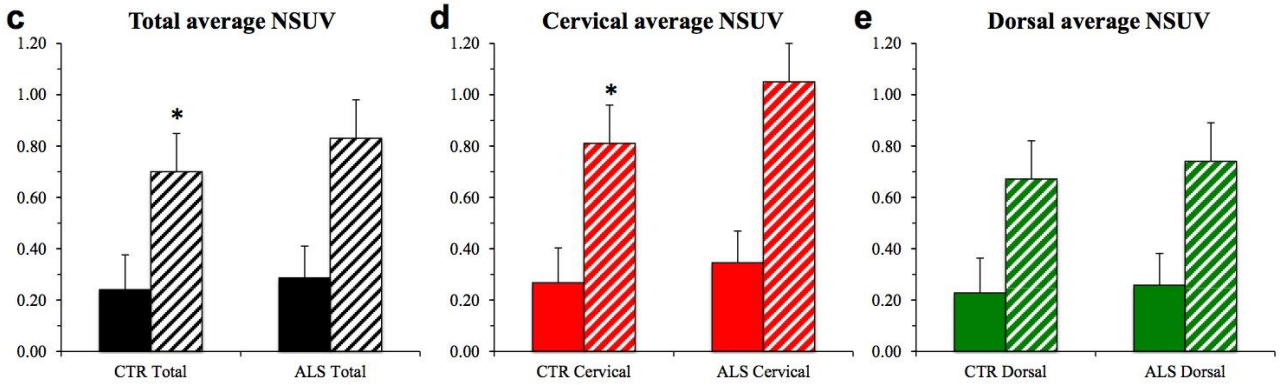
Shape and volume of spinal canal and spinal cord:

No significant differences were observed
in spinal cord and spinal canal volumes between the two groups.

Results (3)

Spinal canal and spinal cord metabolic activity:



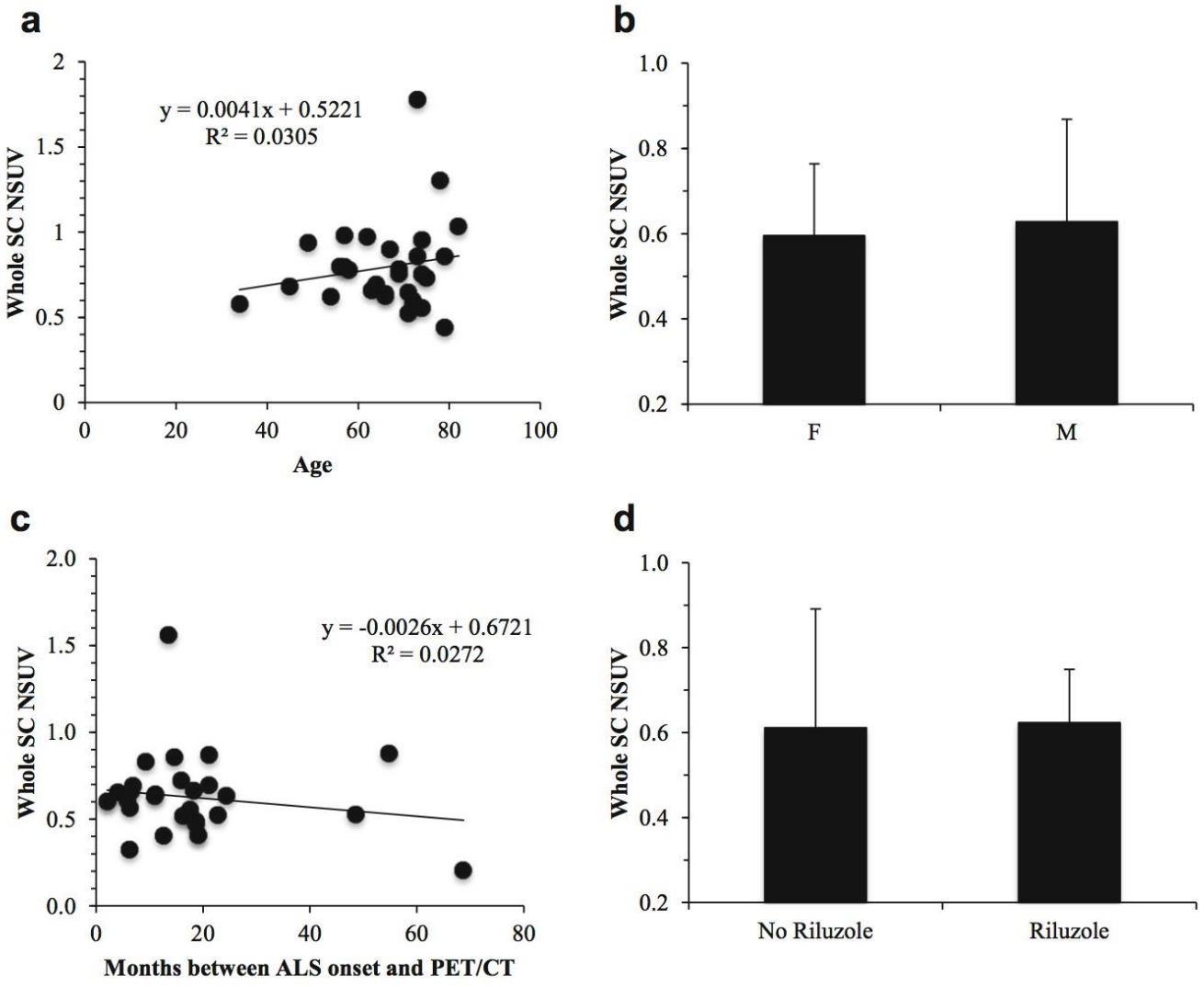


Results (3)

Spinal canal and spinal cord metabolic activity:

F-FDG in the spinal cord was significantly higher in patients than in controls ($p < 0.05$).

Results (4)

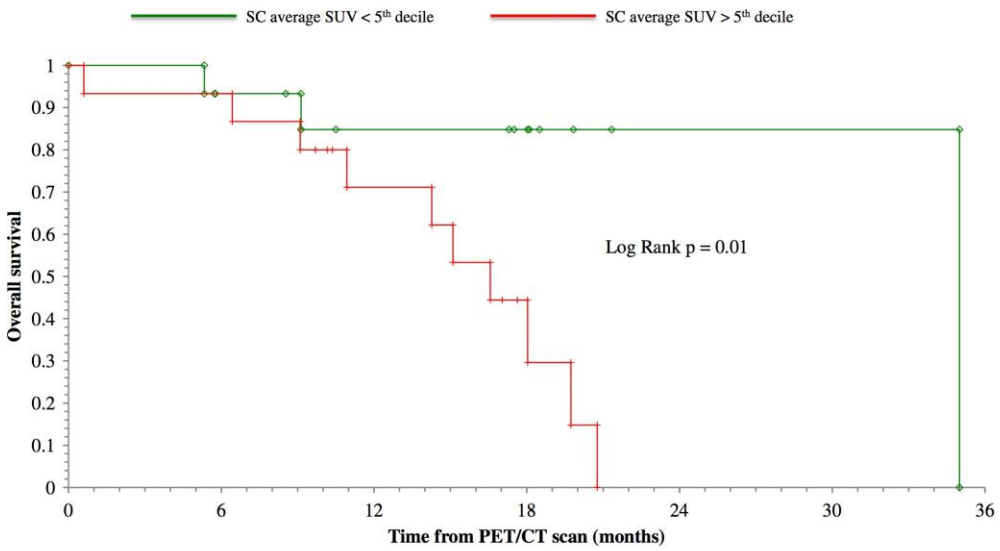

a
y = 0.0041x + 0.5221
R² = 0.0305
Whole SC NSUV
Age
b
Whole SC NSUV
F
M
c
y = -0.0026x + 0.6721
R² = 0.0272
Whole SC NSUV
Months between ALS onset and PET/CT
d
Whole SC NSUV
No Riluzole
Riluzole

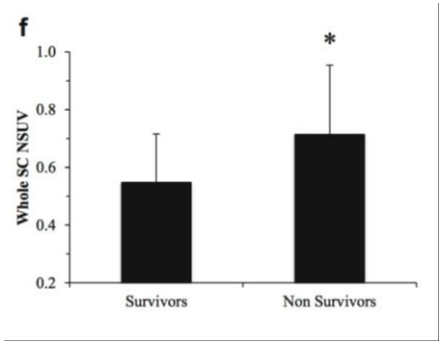
Results (4)

18F-FDG uptake was **completely independent of age, gender**, degree of **functional impairment**, **disease duration** and **riluzole** treatment.

Results (5)

Spinal cord metabolic pattern and patient outcomes:





Results (5)

Spinal cord metabolic pattern and patient outcomes:

Kaplan-Meier analysis showed a **higher mortality rate** in patients with standardized **uptake values above the fifth decile** at the 3-year follow-up evaluation (log-rank test, $p < 0.01$).

Conclusions

This new method enabled the evaluation of spinal cord metabolism and volume and **might represent a potential new window onto the pathophysiology of ALS**

The observation of a **relative increase FDG uptake might reflect inflammatory mechanisms** rather than the expected consequences of motor neuron loss and subsequent spinal cord atrophy.

Perspectives

A new study is currently enrolling patients (50 pts.) in order to:

- optimize image analysis.
- confirm the putative prognostic/diagnostic role of spinal cord (hyper)metabolism in ALS.
- dissect spinal cord metabolism and functional disability.

Future

A role of **spinal cord (FDG) PET/CT** in clinical trials to assess **treatment response?**