Tracking of autologous mesenchymal stem cells after intravenous and intrathecal transplantation in patients with spinal cord injury

JUG M, LEŽAIČ L, SOČAN A, SEVER M, ŠVAJGER U, KOPAČ C, BAJROVIĆ FF

UNIVERSITY CLINICAL CENTRE LJUBLJANA, SLOVENIA

PURPOSE OF THE STUDY

- To investigate safety and feasibility of hybrid SPECT/CT for tracking of bone marrow mesenchimal stem cells (BM MSCs) migration and homing after intravenous and intrathecal application in patients with traumatic spinal cord injury (tcSCI).

- To assess neurologic recovery after BM MSCs transplantation.

MATERIALS AND METHODS

- Patients 18-65 years old with complete tcSCI and early spinal cord decompression were included in the study.
- Patients first received an intravenous transplantation of 150 million allogeneic BM MSC within one month of injury.
- BM MSC were then harvested from patient´s iliac crests and cultivated.
- One month after IV transplantation patients received three intrathecal transplantations of 150 million autologous BM MSC on a monthly basis administered via lumbar puncture.
- BM MSC were labeled with 600MBq of 99mTc-exametazime (HMPAO) and cell migration was evaluated with whole-body planar and hybrid (SPECT/CT) at 1h, 4h and 24h after transplantation.
- Neurologic function was assessed before treatment and one month after each transplantation according to ASIA.
- The clinical protocol is presented in Table 1.

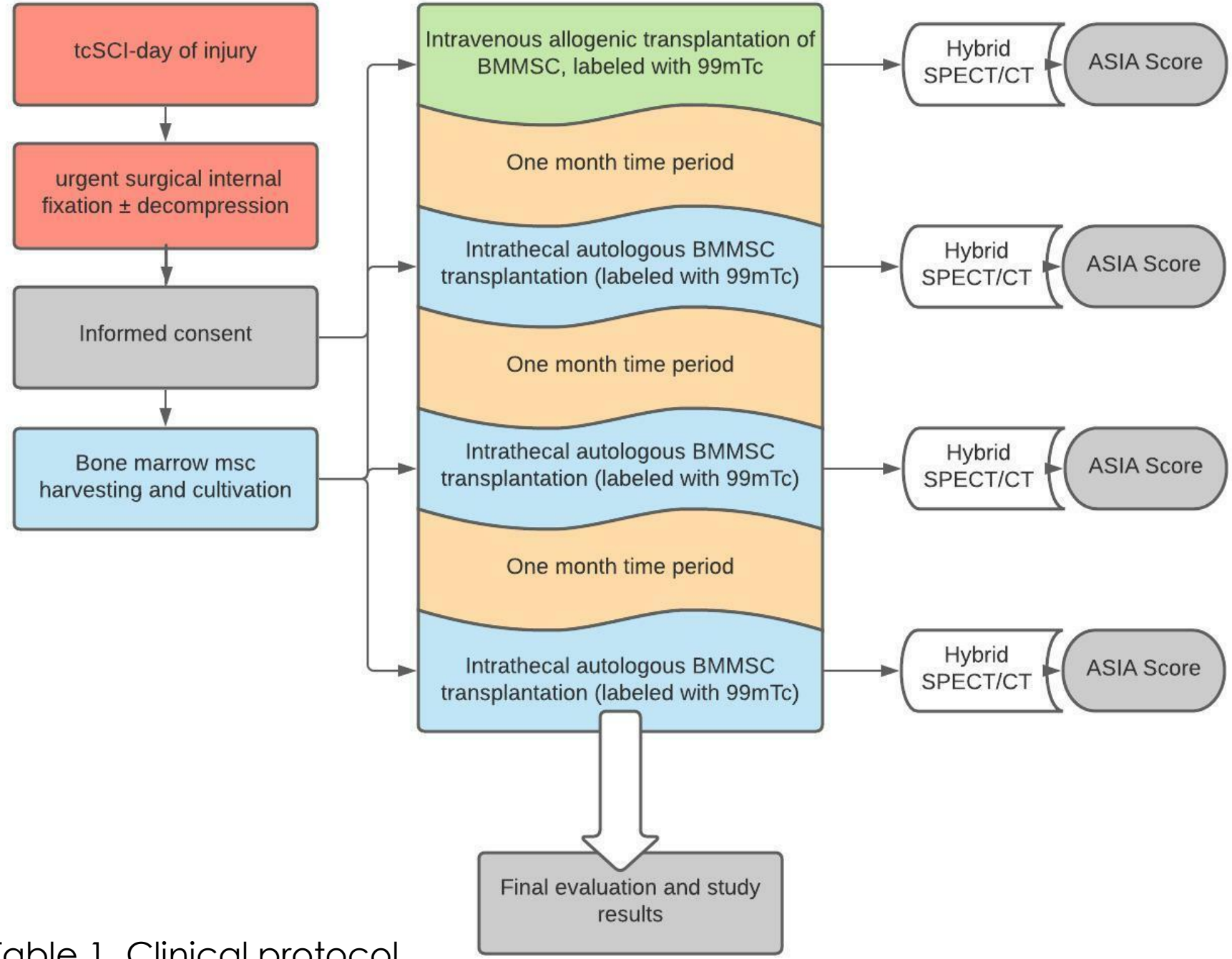

Table 1. Clinical protocol.

RESULTS

- Five male patients from 18 to 58 years of age were included in the study.
- After intravenous administration BM MSC were distributed in the reticuloendothelial system and in the lung parenchyma, whereas BM MSCs retention at the site of spinal cord injury was unremarkable in comparison to intrathecal administration. (Figure 1)
- After intrathecal administration BM MSCs immediately migrated to the site of injury in four out of five patients. (Figure 2) The migration potential was persisted even several months after SCI.
- In a case with insufficient spinal cord decompression due to severe persistent spinal cord edema no homing of BM MSCs at the site of spinal cord injury could be detected. (Figure 3)
- No serious side effects of transplantation and cell labeling were documented.
- Neurologic recovery was seen in 2/5 patients but could not be attributed solely to BM MSCs transplantation. (Table 2)

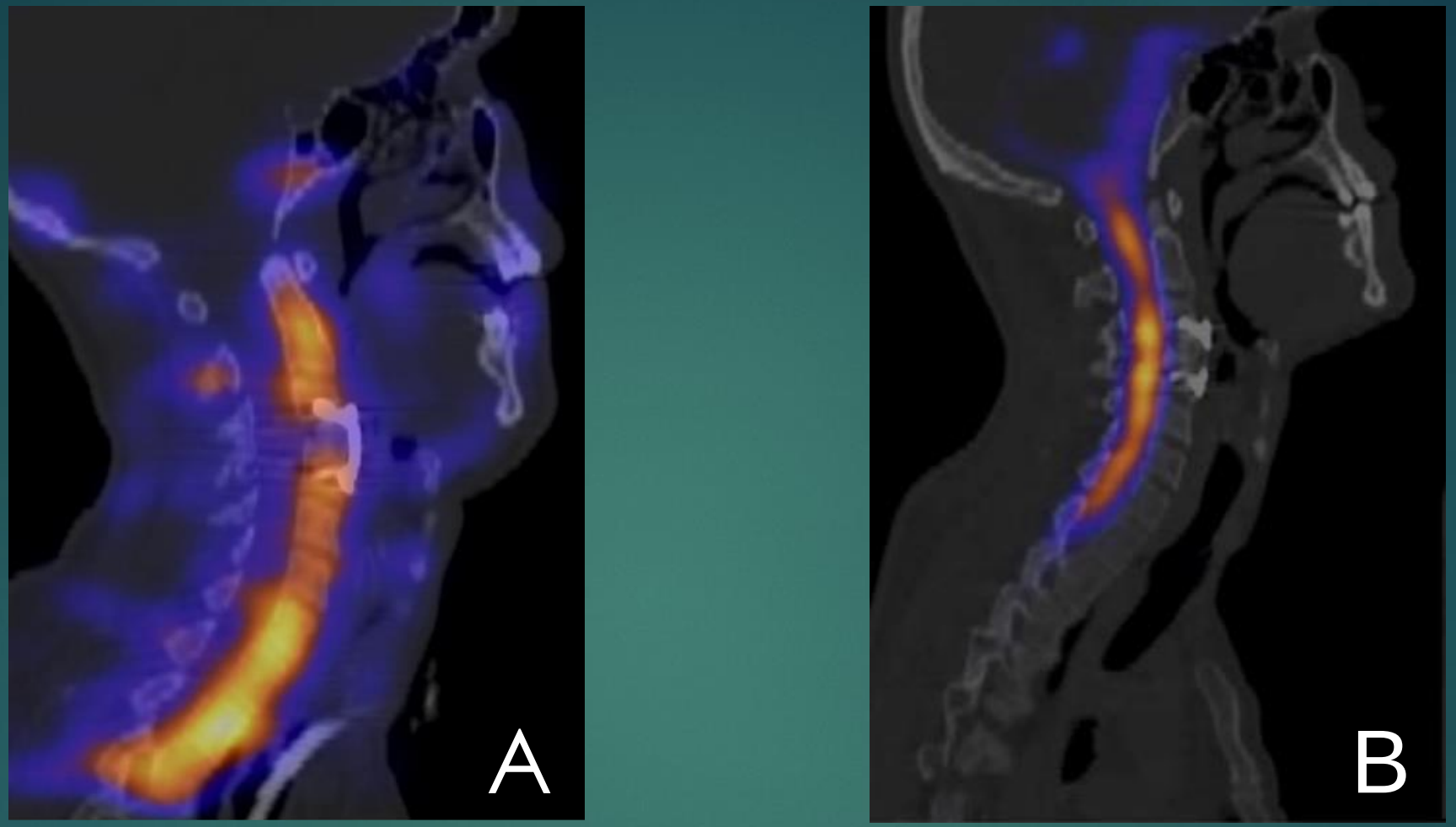

Figure 1.
A**-** Hybrid SPECT/CT imaging of the neck at 4h hours after intravenous administration of radiolabeled MSC three months after acute tSCI at the level C3-C4 showing MSCs in the bone marrow. B- Hybrid SPECT/CT examination showing migration and homing of radiolabeled MSC at the site of tcSCI after intrathecal administration in the same patient.

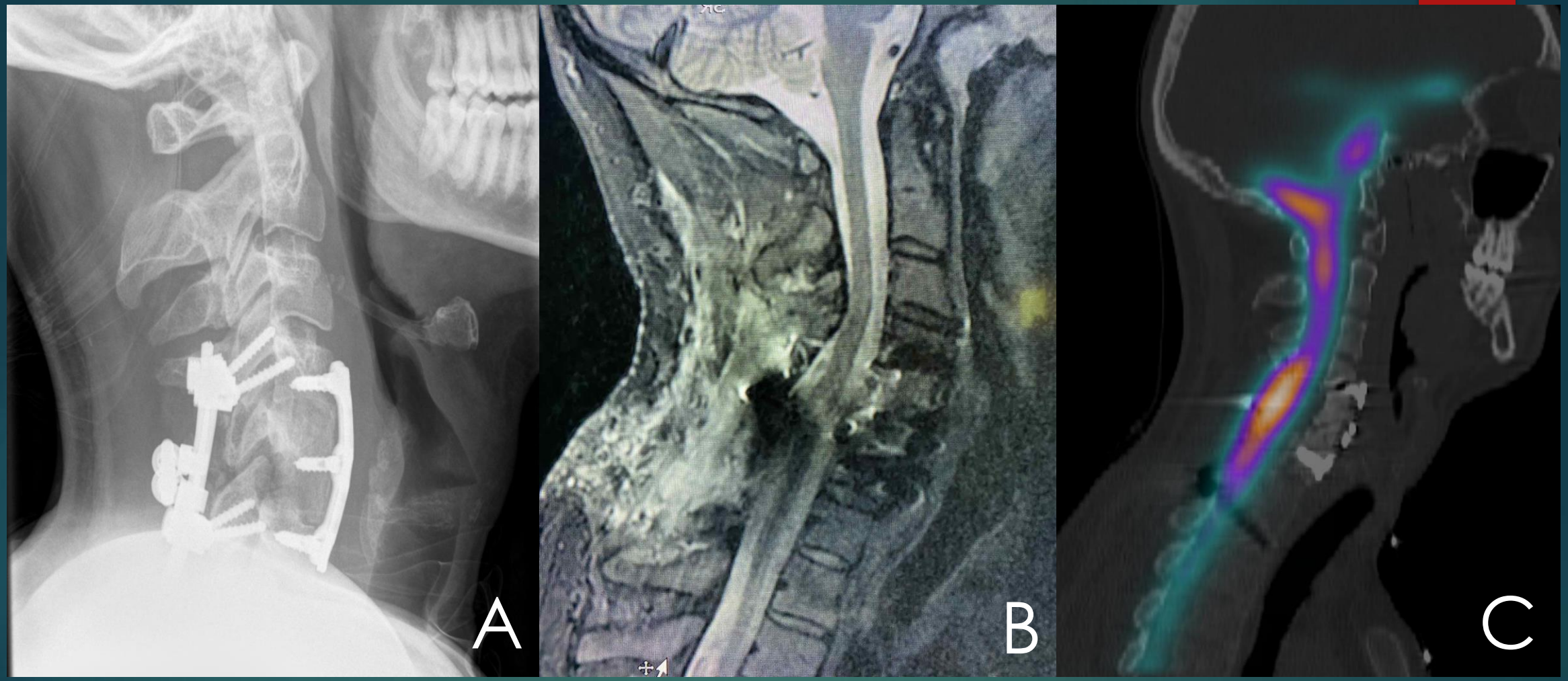

Figure 2.
A- X-ray of cervical spine after corpectomy and 360° fusion with laminectomy at level C4-C6 in a patient with AIS A tcSCI. B- Postoperative MRI before intrathecal BM MSC transplantation showing cerebrospinal fluis surrounding the spinal cord. C- Hybrid SPECT/CT shows accumulation of radiolabeled BM MSC at the site of injury after intrathecal transplantation.

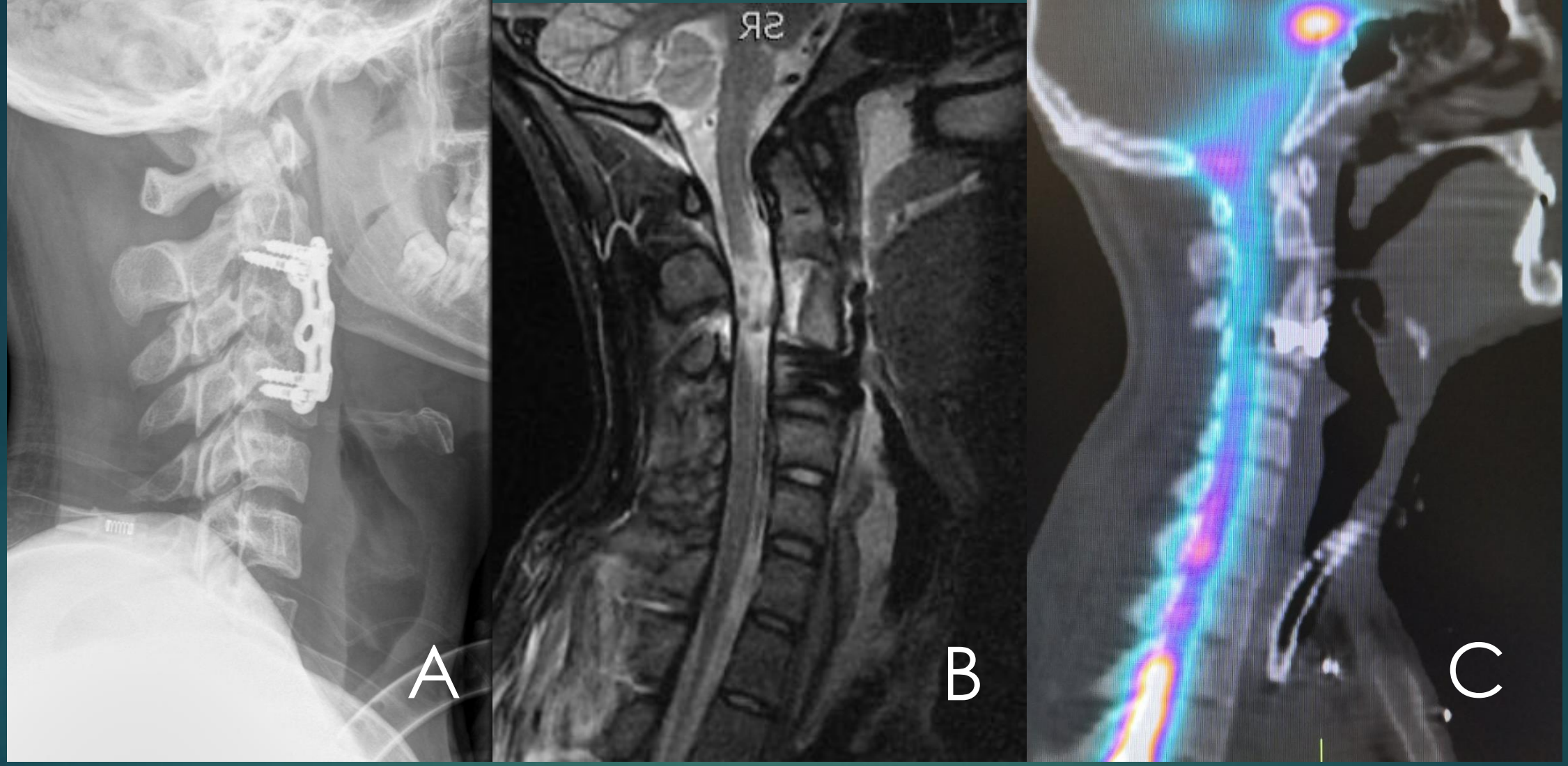

Figure 3.

A- X-ray of the cervical spine after C3 corpectomy and anterior fusion in a patient with AIS A tcSCI. B- Postoperative MRI of cervical spine one month after injury showing severe myelopathy and edema of the spinal cord at the site of injury with reduced spinal fluid circulation. C- Hybrid SPECT/CT after BM MSCs transplantation shows no acummulation of transplanted cells at the site of injury but retention in the thoracic region.

Neurologic recovery

PATIENT	LEVEL	AIS prior to BM MSCs TRANSPLANTATION	AIS one motnh after last BM MSCs transplantion	Major adverse events
32y M	C3	A	A	none
18y M	C3	A	A	none
46y M	C4	A	C	none
58y M	C6	A	B	none
23y M	C5	A	C	none

Table 2. Neurological recovery in patients before transplantation and at study completion.
AIS (ASIA impairment Scale); BM MSC- bone marrow mesenchimal stem cells

CONCLUSIONS

- Hybrid SPECT/CT imaging is safe and can be used for tracking migration of BM MSCs.
- Retention of cells at the site of spinal cord injury is superior after intrathecal than after intravenous administration.
- BM MSCs may migrate to the site of SCI after transplantation even months after injury.
- Severe cord edema and/or insufficient decompression may prevent cell migration and homing, probably due to spinal canal obliteration and reduced spinal fluid circulation.
- Sufficient decompression confirmation on MRI is suggested before intrathecal cell transplantation.