

Clinical effect of intrathecal infusion of allogeneic mesenchymal stem cells derived from umbilical cord Wharton's jelly (WJ-MSC) in adults with spinal cord injury (SCI) treated at BioXcellerator, Medellín, Colombia

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Introduction

SCI is a public health problem worldwide. SCI is characterized by the presence of permanent or partial neurological damage and there is no definitive treatment. Multiple therapeutic alternatives are currently being developed for these lesions, and Stem cell therapy including WJ-MSC, could improve SCI by modulating the inflammatory response

Objective

The aim was to describe the clinical effect of intrathecal WJ-MSC therapy

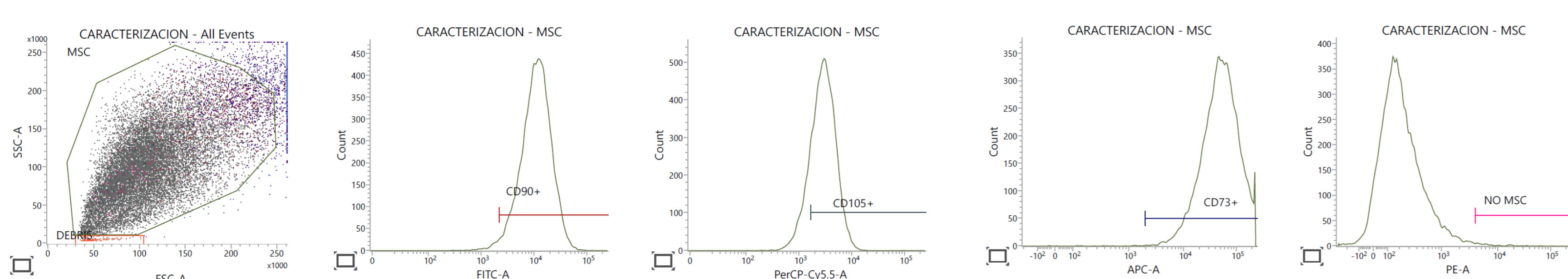
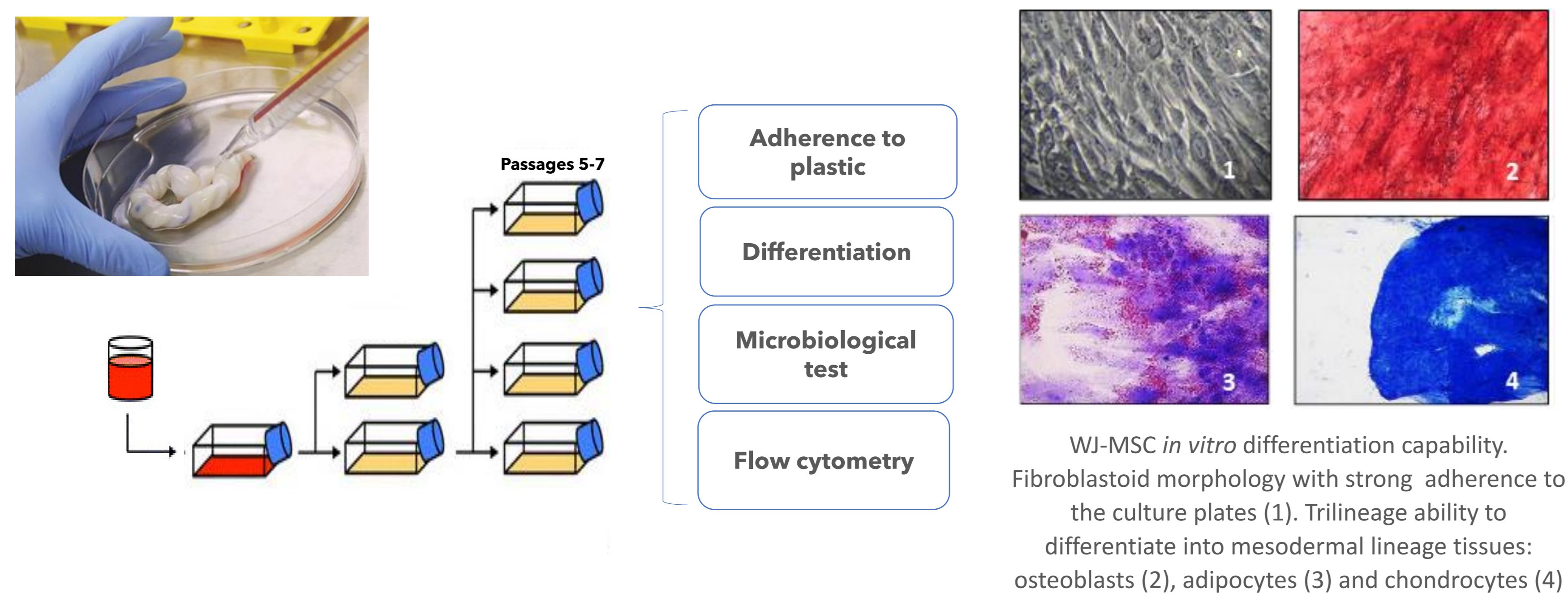
Materials and methods

A retrospective cohort was followed by using ASIA scale at 3, 6, 9 months post-treatment and this study was approved by an ethics committee. Informed Consent was signed for each patient included.

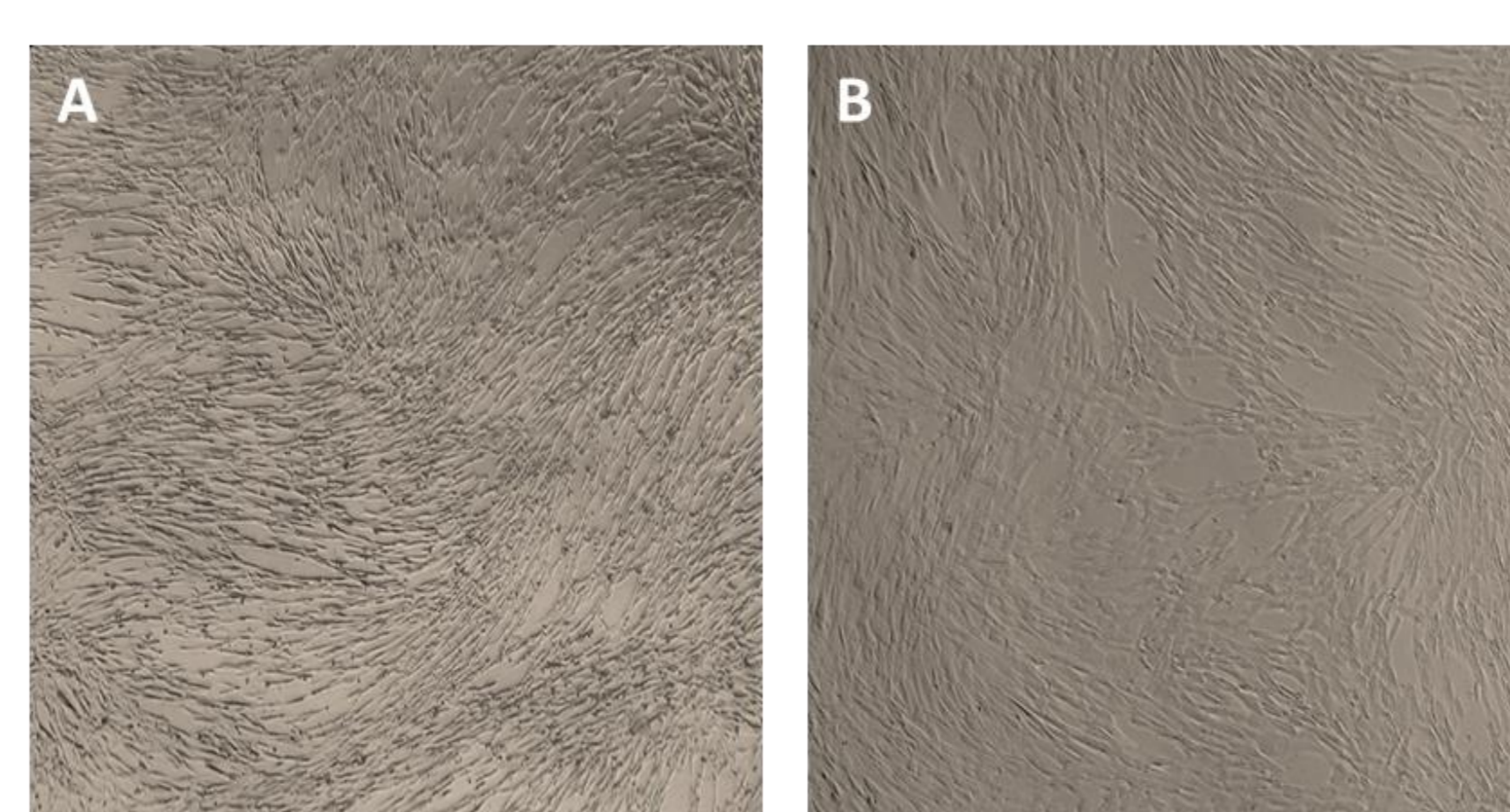
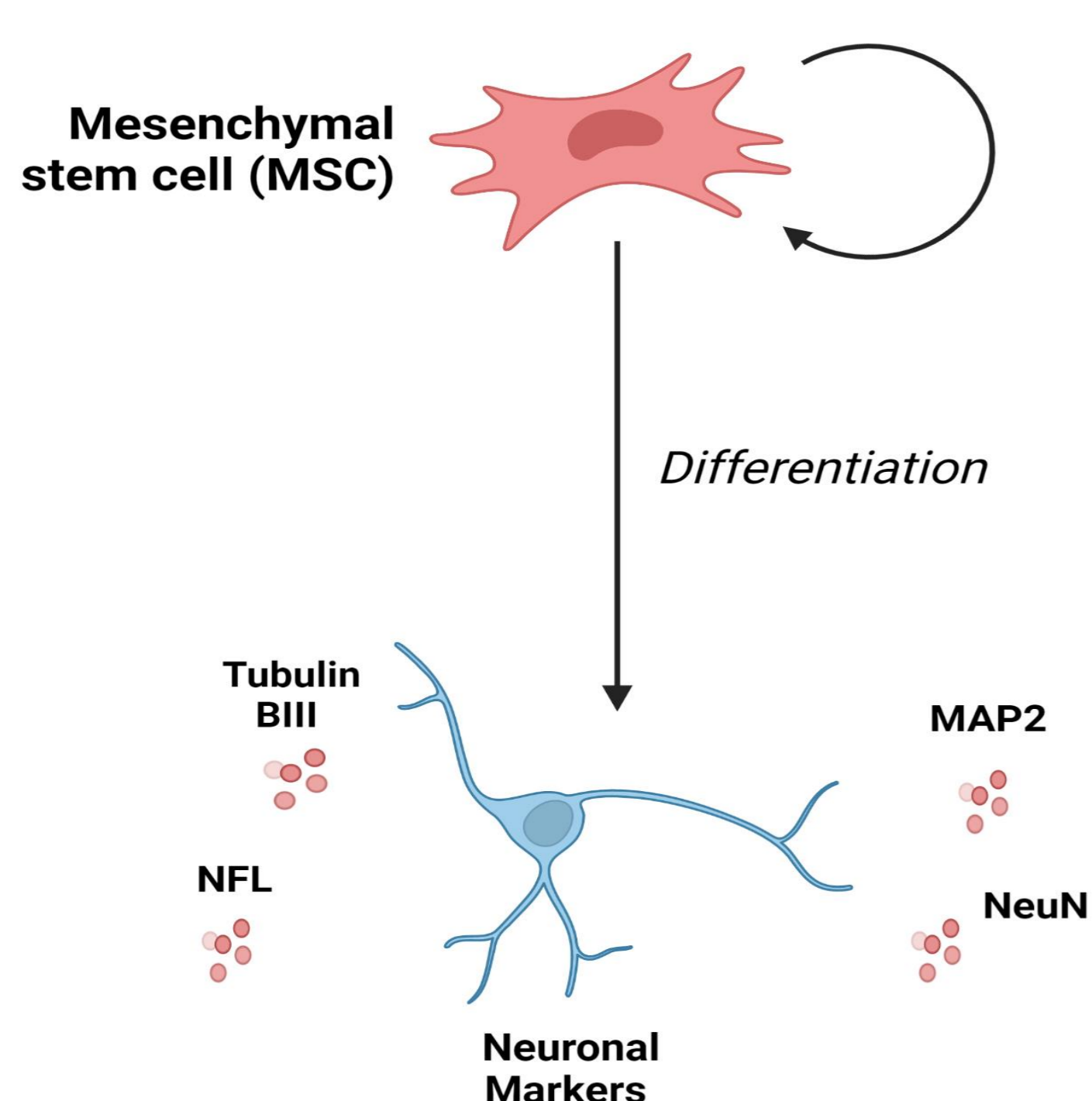
In vitro: WJ-MSC were obtained using the explant method and expanded until passage 7. Cell-markers expression, *in vitro* differentiation to mesodermal lineage and microbiological tests were conducted. WJ-MSC were cultured in cerebrospinal fluid (CSF) for 72 hours, and cell markers expressions of Tubulin β -III, NeuN, Neurofilament light (NFL) protein and MAP2 were evaluated.

In vivo: Treatment protocol included two intrathecal applications of $4,0 \times 10^7$ IT and $2,0 \times 10^7$ intravenous WJ-MSC. Cell therapy was repeated two to four times every three months. An ethics committee approved the research protocol and the patients signed informed consent.

In vitro results: Obtention and characterization of WJ-MSC



In vitro results: Expression profile of nerve-like cells markers



	β III Tubulin	MAP2	NFL	NeuN
Control WJ-MSC	93,0%	30,5%	13,0%	4,5%
CSF WJ-MSC	96,0%	73,5%	98,0%	98,5%

Expression of nerve-like markers in WJ-MSC cultured in CSF. WJ-MSC cultured in 50% CSF expressed nerve-like markers over 73% compared to less than 30% of cells cultured in medium with 10% hPL

In vivo results: Safety and efficacy

- ✓ A total of 11 patients were included (October/2019-January/2022) with 4 treatments sessions completed. Female (n=2, 18.2%), Male (n=9, 81.8%)
- ✓ Complete injuries (n=8) 72,7%
- ✓ No serious adverse events were reported. WJ-MSC are safe and seem to have valuable clinical effects in SCI patients

Descriptives

Age	length of WJ-MSC treatment time (months)	Total time of SCI (months)	Months post-trauma until the first treatment	AIS motor score upper limbs T1	AIS motor score lower limbs T1	AIS light touch score T1	AIS pin prick score T1	AIS motor score upper limbs T2	AIS motor score lower limbs T2	AIS light touch score T2	AIS pin prick score T2	AIS motor score upper limbs T3	AIS motor score lower limbs T3	AIS light touch score T3	AIS pin prick score T3	AIS motor score upper limbs T4	AIS motor score lower limbs T4	AIS light touch score T4	AIS pin prick score T4
Mean	34,5	18,9	43,5	24,5	36,8	4,27	62,2	58,5	35,2	6,45	56,4	40,1	5,91	64,1	63,7	38,7	6,73	72,5	72,1
Median	33	15	38	21	50	0	72	56	40	0	50	50	0	62	60	50	0	80	80
Standard deviation	13,7	9,59	15,3	16,9	19,5	8,13	24,3	24,8	17,6	9,68	21,4	22,3	17,5	11,1	24,8	26,3	17,0	13,7	28,5
IQR	12,0	7,50	18,5	23,5	26,5	3,00	40,5	43,0	29,5	12,5	34,5	36,0	21,5	5,50	38,0	40,5	23,0	4,00	41,5
Range	42	27	45	50	50	21	64	69	50	29	59	61	54	34	67	76	46	42	80
Minimum	20	11	20	2	0	0	28	23	0	0	32	30	6	0	34	29	4	0	32
Maximum	62	38	65	52	50	21	92	92	50	29	91	91	60	34	101	105	50	42	112

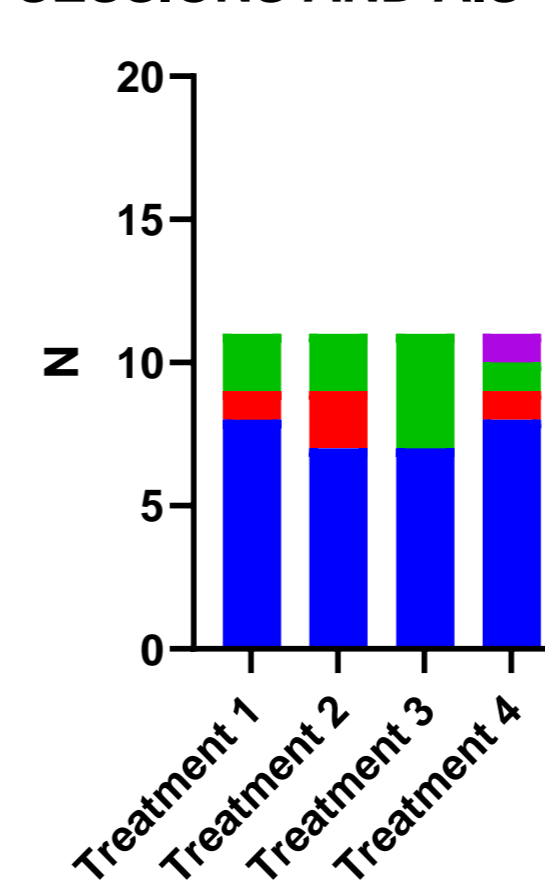
Frequencies of Type of imaging injury

Type of imaging injury	Counts	% of Total	Cumulative %
Edema	1	9.1 %	9.1 %
Myelomalacia/myelopathy	1	9.1 %	18.2 %
Undetermined	9	81.8 %	100.0 %

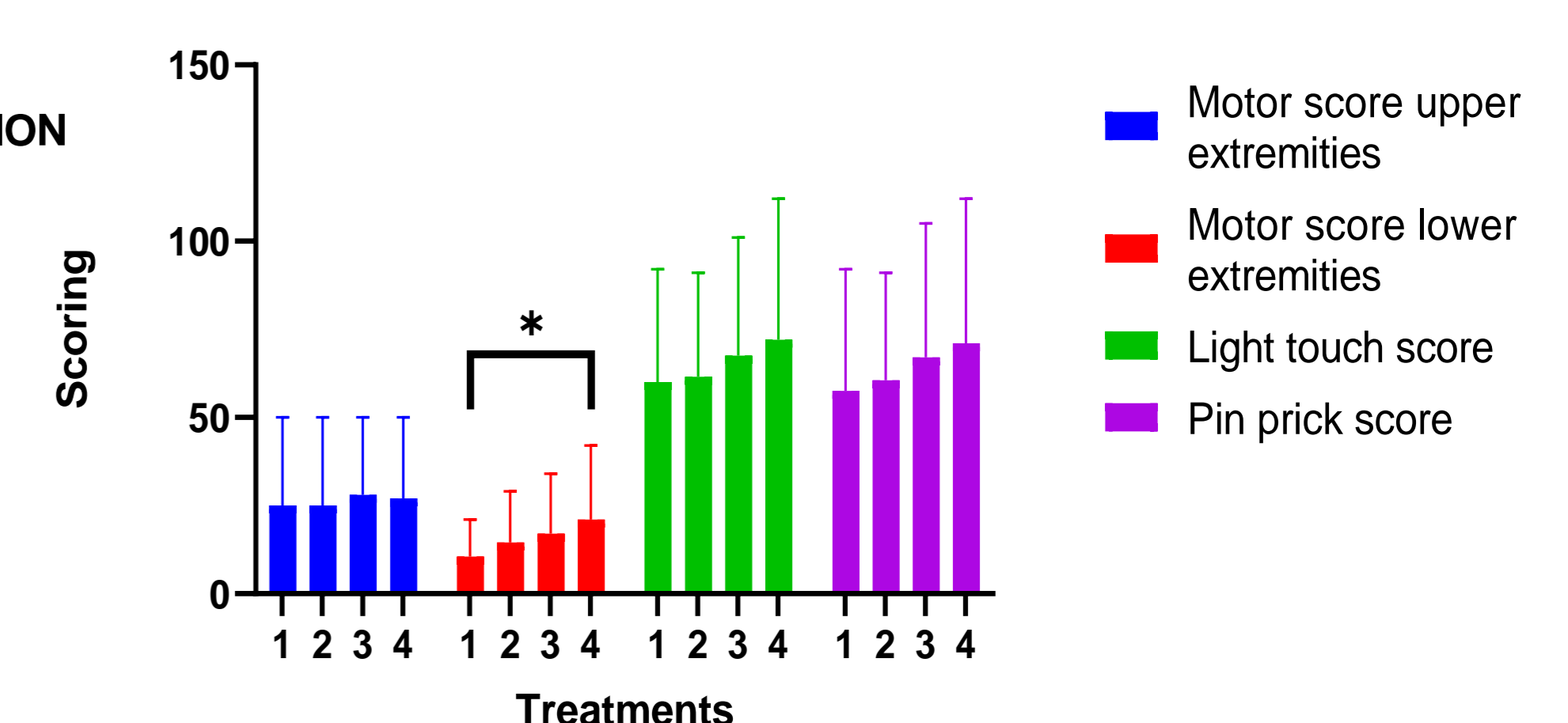
Frequencies of Injury level

Injury level	Counts	% of Total	Cumulative %
Cervical	5	45.5 %	45.5 %
Lumbar	1	9.1 %	54.5 %
Toracic	5	45.5 %	100.0 %

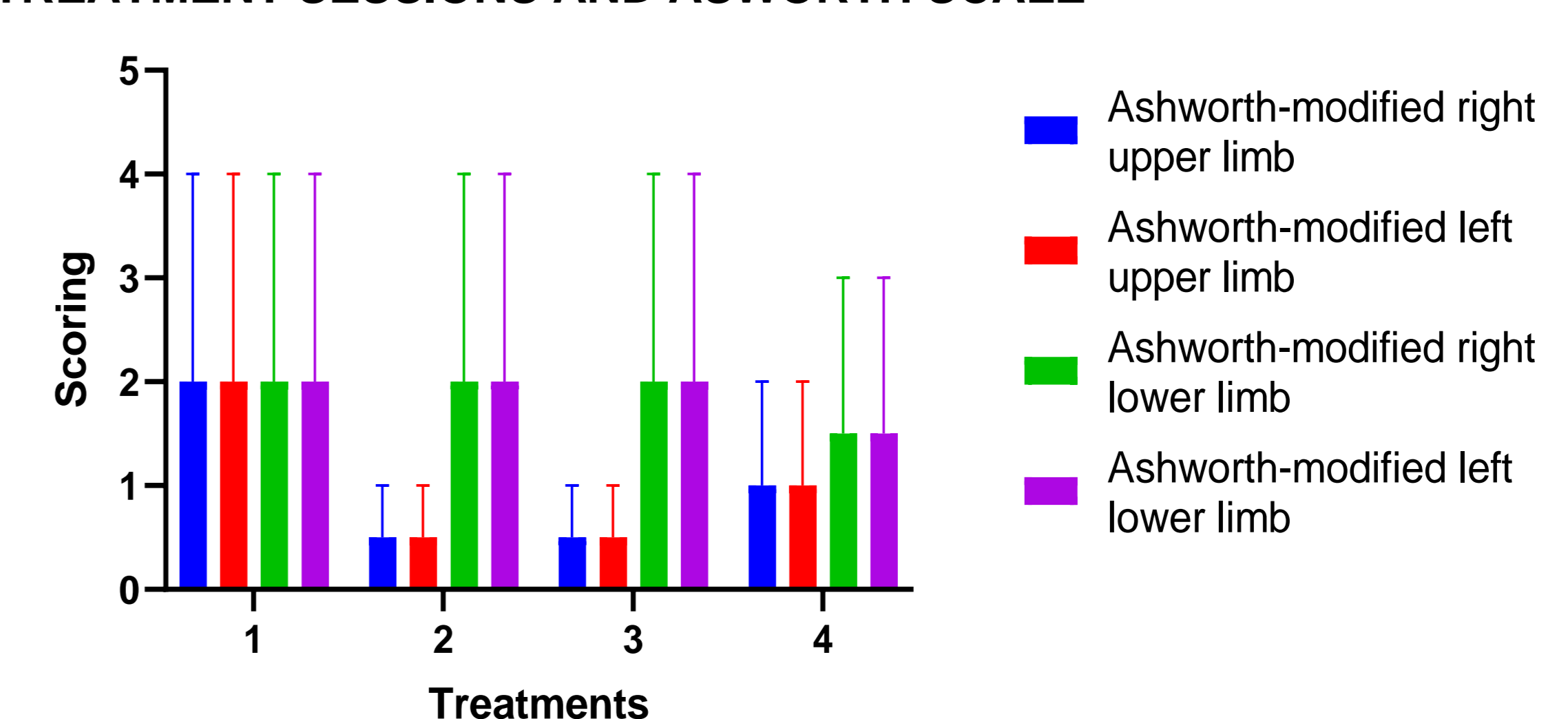
TREATMENT SESSIONS AND AIS GRADE EVALUATION



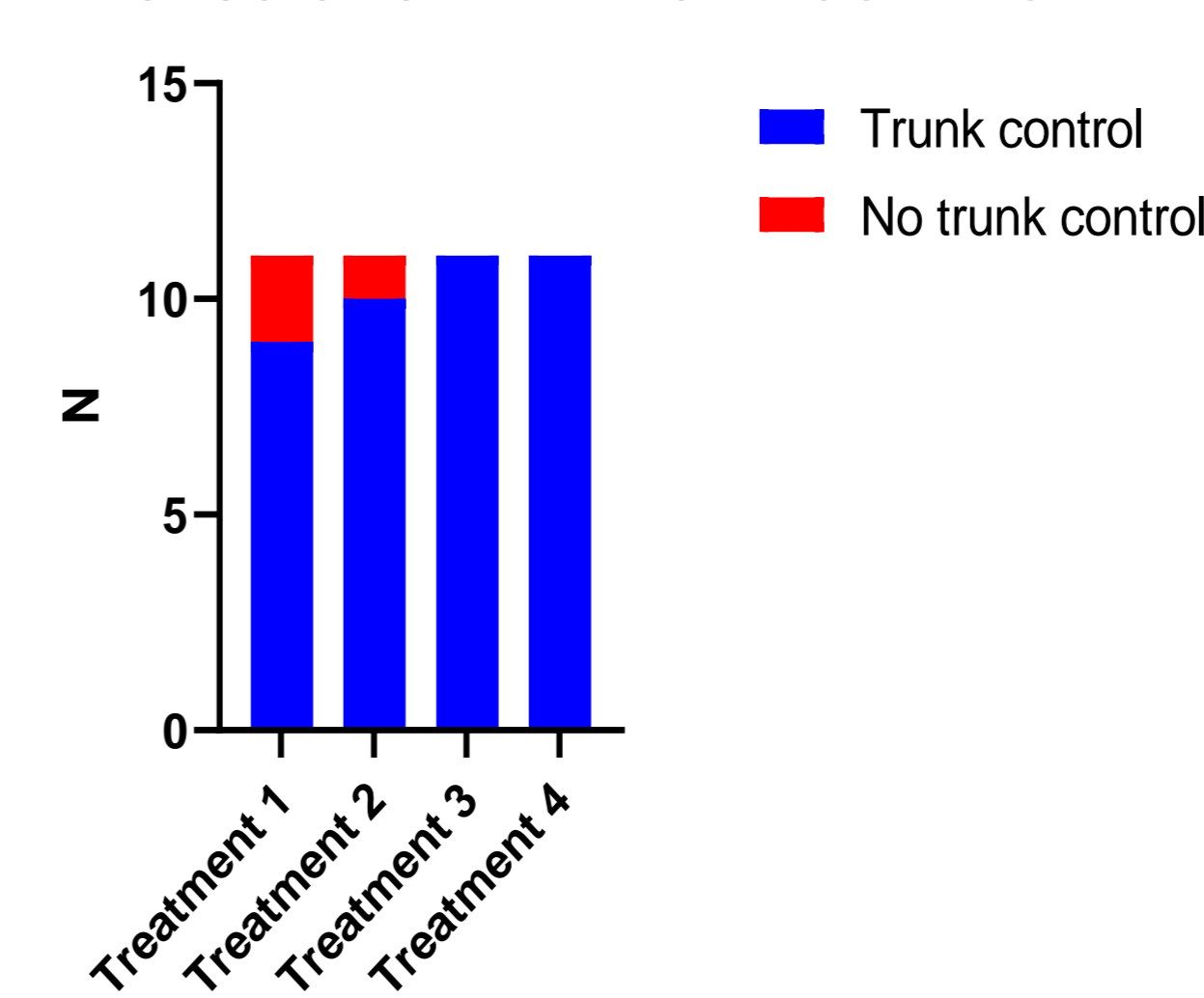
TREATMENT SESSIONS AND ASIA SCORES



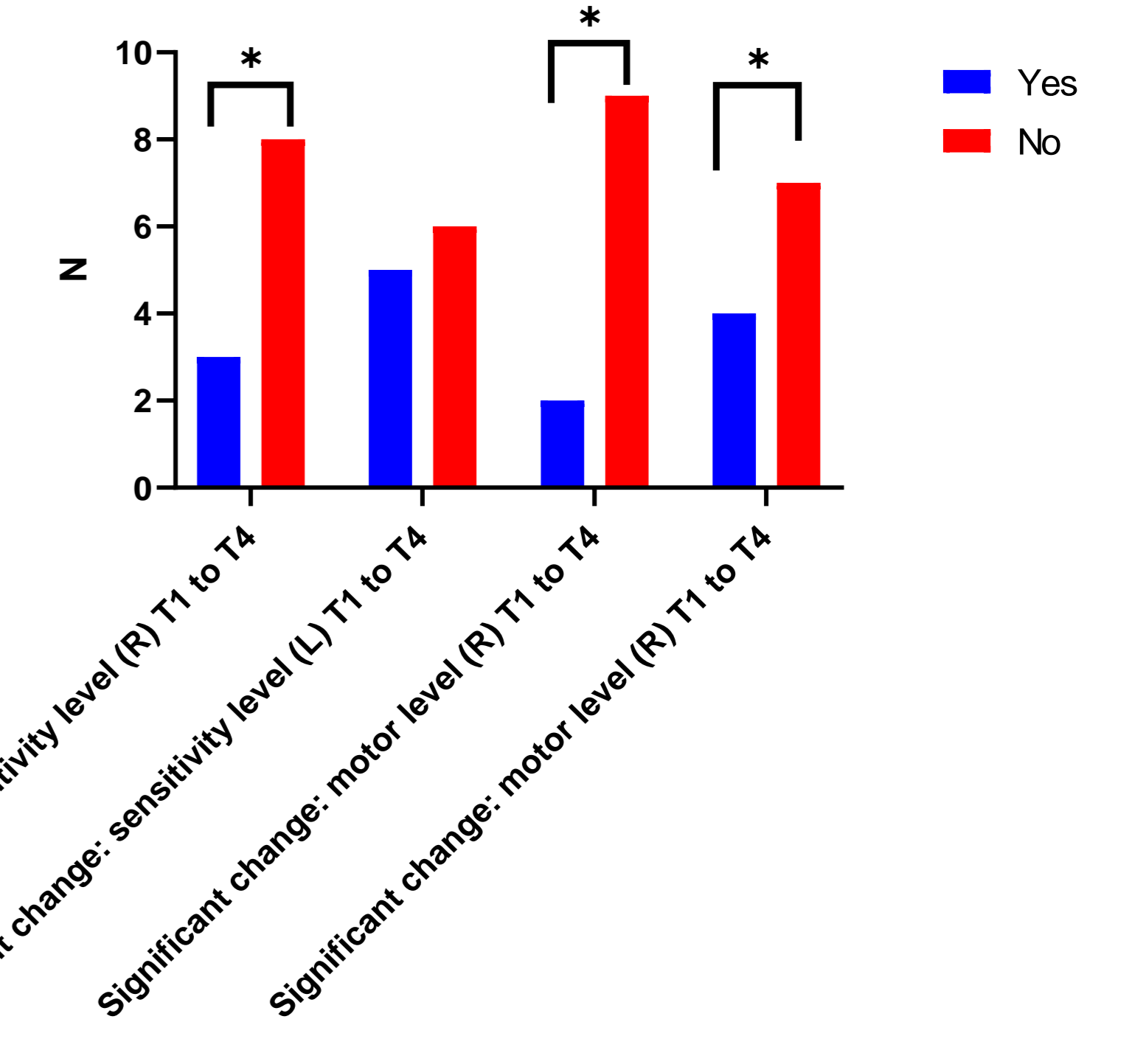
TREATMENT SESSIONS AND ASWORTH SCALE



TREATMENT SESSIONS AND TRUNK CONTROL



NEUROLOGICAL LEVEL CHANGES BETWEEN T1 TO T4



Conclusion

WJ-MSCs meet the criteria of the International Society for Stem Cell Therapy (ISCT) and, the results obtained suggest clinical evidence of regenerative capacity through improvement in somatosensory and motor sensitivity in patients with SCI

Bibliography

Albu S, Kumru H, Coll R, Vives J, Vallés M, Benito-Penalva J, et al. Clinical effects of intrathecal administration of expanded Wharton jelly mesenchymal stromal cells in patients with chronic complete spinal cord injury: a randomized controlled study. *Cytotherapy*. 2021 Feb;23(2):146-156. doi: 10.1016/j.jcyt.2020.08.008.