

## ADCON Studies

### SPINE

#### A. Cell culture analysis and Animal studies: in chronological order

##### **1. Adcon-L: a review of its development, mechanism of action and preclinical data.**

Frederickson RC.

Gliatech Inc., Cleveland, OH, USA.

Eur Spine J **1996**; 5 Suppl 1: S7-9

*Summary: scientific rationale based on certain properties of glial cells and the role and nature of the basal lamina. Evaluation in laminectomy model in rats and discectomy model in dogs. In all studies, Adcon-L was effective barrier to peridural scar and surgical adhesions.*

##### **2. Reduction of peridural fibrosis after lumbar laminectomy and discectomy in dogs by a resorbable gel (Adcon-L).**

Einhaus SL, Robertson JT, Dohan FC Jr, Wujek JR, Ahmad S.

Dept Neurosurg, Univ of Tennessee, Memphis, TN, USA.

Spine **1997** Jul 1;22(13):1440-7

*Summary: 7 adult dogs underwent three level unilateral lumbar laminectomy and anular fenestration, Adcon-L applied to two randomly assigned sites, third site: sham surgery. Results: reduction of local peridural fibrosis without negative impact on healing.*

##### **3. Use of Adcon in neurosurgery: preclinical review.**

Lo H, Frederickson RC.

Gliatech Inc., Cleveland, OH, USA

Neurol Res **1999**; 21 Suppl 1:S27-32

*Summary: review of animal models (mostly rats). In all studies Adcon-L and Adcon-T/N were safe and effective barriers to post-operative peridural and perineural fibrosis.*

##### **4. Prevention of epidural fibrosis with Adcon-L in presence of a durotomy during lumbar disc surgery: experiences with a pre-clinical model.**

Robertson JT, Maier K, Anderson RW, Mule JL, Palatinsky EA.

Dept Neurosurg, University of Tennessee, Memphis, TN, USA

Neurol Res **1999**; 21 Suppl 1:S61-6

*Summary: results demonstrate in a rat model that Adcon-L does not interfere with normal dural healing process following meningeal puncture or dural incisions.*

**5. A reservable antiadhesion barrier gel reduces the perineural adhesions in rats after anastomosis.**

Isla A, Martinez JR, Perez-Lopez C, Perez Conde C, Morales C.

Dept Neurosurg, La Paz University Hosp, Madrid, Spain

J NeurosurgSci. 2003 Dec; 47(4): 195-200.

*Summary : randomized controlled study with application of Adcon gel versus no treatment around a previously exposed and then anastomosed peripheral nerve in a rat model. Results demonstrate decreased fibrosis around nerve anastomosis sites while growth between severed ends of axons was not impeded.*

**6. Inhibition of spinal fusion by use of a tissue ingrowth inhibitor.**

Zou X, Li H, Egund N, Lind M, Bungler C.

Orthopaedic Research Laboratory, Aarhus University Hosp, Aarhus, Denmark

Eur Spine J. 2004 March; 13(2): 157-63.

*Summary: In a single-level intertransverse arthrodesis model in pigs, Adcon gel mixed into autogenous bone graft was found to delay or decrease bone formation. This accords with the authors' hypothesis that the use of Adcon gel can prevent the occurrence of spontaneous fusion in very young scoliosis patients.*

B. Human studies : in reverse chronological order

1.

[J Neurol Neurosurg Psychiatry](#). 2005 Jul;76(7):1031-3.

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**Bilateral subdural haematomata and lumbar pseudomeningocele due to a chronic leakage of liquor cerebrospinalis after a lumbar discectomy with the application of ADCON-L gel.**

[Kuhn J](#), [Hofmann B](#), [Knitelius HO](#), [Coenen HH](#), [Bewermeyer H](#).

Department of Neurology, Kliniken der Stadt Köln, Krankenhaus Merheim, Ostmerheimerstrasse 200, D-51109 Cologne, Germany. [Kuhnj@kliniken-koeln.de](mailto:Kuhnj@kliniken-koeln.de)

The anti-adhesion gel ADCON-L has been available since the end of the 1990s. During disc surgery it can be applied to the spinal nerve roots and the dura mater spinalis in order to inhibit fibroblast migration and thus avoid postoperative adhesions or excessive keloids, respectively. Due to the way ADCON-L works, inadvertent, intraoperative dural lesions may stay open much longer than usual because ADCON-L inhibits the natural healing process. Possible consequences are a chronic leakage of cerebrospinal fluid in combination with intracranial hypotension syndrome. We report on a patient who underwent lumbar disc surgery with application of ADCON-L gel. Postoperatively he suffered from acute headache, nausea, and vomiting. A lumbar pseudomeningocele was demonstrated on magnetic resonance imaging (MRI). Furthermore, cranial MRI revealed bilateral, chronic subdural haematomata which indicated intracranial hypotension syndrome or continuous leakage of cerebrospinal fluid at the lumbar site. With conservative treatment the problems were gradually reduced and eventually the subdural haematomata were no longer detected. The pseudomeningocele persisted over a 4 month period of observation. Because of the complications we found, the local application of ADCON-L during lumbar disc surgery should be critically evaluated.

**2. Adcon-L gel and intraoperative hypotension during lumbar discectomy.**

McAuley D, Russell C, Farling P.

Dept Neurosurg, Royal Victoria Hospital, Belfast, N.Ireland.

Br J Neurosurg 2004 Apr;18(2):180-2

*Summary: Case report describing an intraoperative hypotensive event associated with application of Adcon gel during lumbar surgery*

**3. Two-year results after lumbar microdiscectomy with and without prophylaxis of a peridural fibrosis using Adcon-L.**

Ganzer D, Giese K, Volker L, Pietzner U, Follak N, Merk H.

Dept Orthopaedics, Dietrich Bonhoeffer Klinikum, Neubrandenburg, Germany

Arch Orthop Trauma Surg **2003** Feb; 123(1):17-21

*Summary : retrospective, 46 patients Adcon-L, 46 control, 24 MRI, no significant clinical difference between groups, not enough MRI data.*

**4. Use of Adcon-L to prevent peridural fibrosis following re-operation for recurrent lumbar radiculopathy: clinical results.**

Kessel G, Bocher-Schwarz HG, Schwarz M.

Dept Neurosurg, Johannes Gutenberg University of Mainz, Germany

Minim Invasive Neurosurg **2002** Sep; 45

*Summary: retrospective, Adcon-L applied in lumbar scar resection gives better clinical outcomes- investigations needed to identify clinical and radiographic predictive factors.*

**5. Efficacy of the morphine-Adcon-L compound in the management of postoperative pain after lumbar microdiscectomy.**

Mastronardi L, Pappagallo M, Puzzilli F, Tatta C.

Div Neurosurg, Sandro Pertini Hospital, Rome, Italy

Neurosurgery **2002** Mar;50(3):518-24

*Summary: randomised, controlled, double-blind, 100 patients, Adcon-L as vehicle to administer 1mg Morphine epidurally in lumbar microdiscectomy: Safe, effective, significant analgesic and rapid functional improvement*

**6. The Use of Adcon-L - adhesion control in a barrier gel – in spinal surgery.**

Tobler W.

Dept Neurosurg, Mayfield Clinic and Spine Institute, The Neuroscience Institute, Cincinnati, OH, USA.

Review sponsored by Gliatech Inc., **2001**.

*Summary: review – conclusion: first product with demonstrated clinical merit for prevention of symptomatic post-operative epidural fibrosis in lumbar surgery. Easily applied, does not require significant additional time or effort.*

**7. Adcon-L for inhibition of post-operative peridural fibrosis following spinal root decompression : a retrospective clinical data review.**

Greenspan J, Sybert G, Maroon J, Bartie B, Moldawer T, Ma F, Tedford C, Palatinsky E, Fournier M, Lavin P, Beghin J, Rouben D, Kolavo j, Shugart R, Mathern B. North County Neurosurgical Associates, NY, USA, The Sybert Institute, FL, St. Croix Orthopaedics, MN, Southern California Orthopaedic Institute, CA, Tristate Neurosurgical Associates UPMC, PA, Gliatech Medical Inc., Boston Biostatics, Inc., Indiana Back Center, IN, River City Orthopaedic Surgeons, P.S.C., KY, orthopaedic Associates of DuPage, IL, fort Wayne Orthopaedics, IN, Mid-Atlantic Spine Specialists, VA, USA.

US retrospective clinical study, data with Gliatech, Inc. Review and poster presentation. Data from surgeries **between June 1, 1998 and Oct 30, 2000.**

*Summary: retrospective review of postop outcome, 10 centers, total 847 Adcon-L patients, no adverse events 'probably' or 'definitely' related to Adcon-L, adverse events 'possibly' related to Adcon-L in 16.7% but incidence of CSF leakage or pseudomeningocele only in 0.6%: conclusion Adcon-L is safe. Re-operations in 4.3% for reherniation or retained disc fragment: 74.3% showed no significant peridural fibrosis. Results consistent with prospective, randomised, controlled European study.*

**8. Adcon-L and hypotension during lumbar microdiscectomy.**

Kalogrianitis S, Barrett P, Shackelford I.

Dept Musculoskeletal Science, Royal Liverpool University Hospital, UK

Br J Anaesth **2001** Nov; 87(5): 770-1

*Summary: adverse haemodynamic reactions (hypotension) in 7/212 patients (3.3%) >> dosage min 3g!*

**9. Spinal epidural fibrosis following lumbar discectomy and anti-adhesion barrier. (article in Spanish)**

Isla A, Alvarez F.

Servicio de Neurocirurgia, Hospital La Paz, Madrid, Spain.

Neurocirurgia (Astur) **2001** Oct ;12(5) :439-46

*Summary : multicentric, double blind, 253 patients, no clinical difference at 6 months, absence of fibrosis at reoperation.*

**10. RE: Unrecognized durotomy after lumbar discectomy: a report of four cases associated with the use of Adcon-L.**

Kramer KM.

University Hospital Düsseldorf, Germany.

Spine **2001** Nov 1; 26(21): 2405 Comment on Spine 2001 Jan 1; 26(1): 115-8

**11. Results of applying Adcon-L after lumbar discectomy: the German Adcon-L study.**

Richter HP, Kast E, Tomczak R, Besenfelder W, Gaus W.

Dept Neurosurg, University Ulm, Germany

J Neurosurg **2001** Oct; 95(2 suppl): 179-89

*Summary: randomised, 398 patients, 10% drop-out, focus on patient-oriented endpoints, no significant clinical advantage at 6 months, but slight MRI advantage(6 months)*

**12. Spontaneous postoperative cerebrospinal fluid leaks following application of anti-adhesion barrier gel: case report and review of the literature.**

Hieb LD, Stevens DL.

Spine **2001** Apr 1; 26(7): 748-51

*Summary: retrospective, cases of last 5 years, no control, one surgeon, 5/27 patients with leakag , 3 needed re-operation, all elderly people with spinal stenosis and wafer thin dura, at re-operation no dura thickening because no scar in Adcon treated patients making repair of dura tear difficult. Dosage min 3 g Adcon-L probably too high esp in old people with very thin dura.*

**13. Peridural fibrosis in lumbar disc surgery – pathogenesis, clinical problems and prophylactic attempts (article in Polish).**

Gasinski P, Radek M, Jozwiak J, Lyczak P.

Kliniki Neurochirurgii Szpitala Klinicznego Wojskowej Akademii Medycznej, Poland.

Neurol Neurochir Pol **2000** Sep-Oct; 34(5): 983-93.

*Summary: review on peridural fibrosis and perspectives for Adcon-L*

**14. Unrecognised durotomy after lumbar discectomy: a report of four cases associated with the use of Adcon-L.**

Le AX, Rogers DE, Dawson EG, Kropf MA, De Grange DA, Delamarter RB.  
Spine Institute St John's Health Center, Santa Monica, CA, USA

Spine **2001** Jan 1;26(1):115-8

*Summary: 4 patients with small inadvertent durotomies unrecognised at time of surgery (one at site of previous epidural steroid injection)-Adcon-L may inhibit dural healing and exacerbate CSF leak from microscopic durotomies.*

**15. Perspectives on modern orthopaedics: the use of Adcon-L for epidural scar prevention.**

Fischgrund JS.

William Beaumont Hosp, Royal Oak, Mich., USA

J Am Acad Orthop Surg **2000** Nov-Dec;8(6):339-43

*Summary: review –worthwhile, further studies needed*

**16. Cost effectiveness evaluation of Adcon-L adhesion control gel in lumbar surgery.**

McKinley DS, Shaffer LM.

Gliatech Inc., Cleveland, OH, USA

Neurol Res **1999**; 21 Suppl 1:S67-71

*Summary: economic survey, prospective, randomised controlled study, results at min 12 months: patient satisfaction, return to work, additional medical treatment after surgery, duration of re-operations: significant clinical advantage of Adcon-L for all parameters. Significant economic advantage.*

**17. Inhibition of epidural fibrosis with Adcon-L: effect on clinical outcome one year following re-operation for recurrent lumbar radiculopathy.**

Porchet F, Lombardi D, de Preux J, Pople IK.

Service de Neurochirurgie, CHU Vaudois, Lausanne, Switzerland.

Neurol Res **1999** ; 21 Suppl 1: S51-60.

*Summary: prospective, multicenter, 20 patients, significant improvement of all clinical parameters, no adverse events.*

**18. Prevention of epidural fibrosis in a prospective series of 100 primary lumbo-sacral discectomy patients: follow-up and assessment at re-operation.**

Brotchi J, Pirotte B, De Witte O, Levivier M.

Service de Neurochirurgie, Hôpital Erasme, ULB, Bruxelles, Belgium.

Neurol Res **1999** ; 21 Suppl 1 : S47-50

*Summary: prospective, 100 primary discectomies with use of Adcon-L, 12 months monitoring, 4 re-operations with absent or minimal scar, wound healing excellent.*

**19. Association between peridural fibrosis scar and persistent low back pain after lumbar discectomy.**

Maroon JC, Abla A, Bost J.

Dept Neurosurg, Allegheny General Hosp, Pittsburg, PA, USA

Neurol Res **1999**;21 Suppl 1:S43-6

*Summary: controlled, randomised, double blind multicenter, 298 primary discectomies: Adcon-L patients had significantly less scar on MRI and less back pain at 6 months. Patients with extensive scar reported continuing or debilitating low back pain significantly more often than patients with minimal or no scar, demonstrating a direct correlation between persistent low back pain and extensive scar.*

**20. Association between peridural scar and activity-related pain after lumbar discectomy.**

BenDebba M, Augustus van Alphen H, Long DM.

Dept Neurosurg, John Hopkins School of Medicine, Baltimore, MD, USA

Neurol Res **1999**;21 Suppl 1:S37-42

*Summary: same multicenter study as previous reference now demonstrating less activity related pain through 12 months assessment in the Adcon-L group also having significantly less scar at 1, 6 and 12 months postop.*



**21. MR evaluation of epidural fibrosis; proposed grading system with intra- and inter-observer variability.**

Ross JS, Obuchowski N, Modic MT.

Div Radiology, Cleveland Clinic Foundation, OH, USA.

Neurol Res **1999**;21 Suppl 1:S23-6

*Summary: randomised, double blind, controlled multicenterclinical trial with Adcon-L. MRI reading by two independent blinded readers: substantial intra-observer and nearly perfect inter-observer agreement for evaluation of epidural scar on T1-weighted axial MRI imageswith and without contrast. Standard grading system for epidural scar is proposed.*

**22. Prevention of peridural fibrosis: current methodologies.**

Geisler FH.

Chicago Institute of Neurosurgery and Neuroresearch, IL, USA.

Neurol Res **1999**;21 Suppl 1:S9-22

*Summary: review; cell culture analysis demomstrates that Adcon-L blocks ingrowth of fibroblasts, animal laminectomy models demonstrate major decrease in peridural fibrosis and two multicenter trials (one in Europe with 298 patients and one in the US with 223 patients)show statistically significant positive effect in radiologic index and clinical outcome scores.*

**23. Clinical assessment of a novel anti-adhesion barrier gel: prospective randomised, multicenter clinical trial of Adcon-L to inhibit post-operative peridural fibrosis and related symptoms after lumbar discectomy.**

de Tribolet N, Porchet F, Lutz TW, Gratzl O, Brotchi J, van Alphen HA, van Acker RE, Benini A, Strommer KN, Bernays RL, Goffin J, Beuls EA, Ross JS. Dept Neurosurg,CHU Vaudois, Lausanne, Switzerland,; Dept Neurosurg Kantonsspital Basel, Switzerland; Dept Neurosurg Hop Univ Erasme, ULB, Bruxelles, Belgium; Dept Neurosurg AZ VU Amsterdam, The Netherlands; Dept Neurosurg St Lucas, Amsterdam, The Netherlands; Dept Neurosurg Kantonsspital St.Gallen, Switzerland; Dept Neurosurg Universitätsspital Zürich, Switzerland; Dept Neurosurg, UZ Gasthuisberg, Leuven, Belgium; Dept Neurosurg AZ Maastricht, The Netherlands; Dept Radiology, Cleveland Clinic Foundation, OH, USA.

Am J Orthop **1998** Feb;27(2):111-20

*Summary: significantly better clinical outcomes in Adcon-L group, significant inhibition of peridural scar compared to control, further supported by direct visualisation at re-operation in both groups, no difference in adverse events or wound healing.*

**24. Association between perineural scar and recurrent radicular pain after lumbar discectomy: magnetic resonance evaluation. Adcon-L European study group.**

Ross JS, Robertson JT, Frederickson RC, Petrie JL, Obuchowski N, Modic MT, de Tribolet N.

Div Radiology, Cleveland Clinic Foundation, OH, USA.

Neurosurgery **1996** Apr;38(4):855-61

*Summary: prospective , controlled, randomised, blinded, multicenter, study demonstrates significant association between peridural scar and recurrent radicular pain. Data at 1 and 6 months postop.*

**25. Adcon-L symposium. Round table discussion.**

Robertson JT, Petrie JL, Frederickson RC, de Tribolet N, Hardy R.

Gliatech Inc., Cleveland, OH, USA.

Eur Spine J **1996**; 5 Suppl 1:S26-8

**26. Cost effectiveness of lumbar disc surgery and of a preventive treatment for peridural fibrosis.**

Schwicker D.

HealthEcon, Basel, Switzerland.

Eur Spine J **1996**; 5 Suppl 1:S21-5

*Summary: retrospective approach to predict sequelae, treatment patterns and economic outcomes over a 1-year period following primary surgery with or without Adcon-L for lumbar herniated disc: in the Adcon-L group the quality of surgical outcome improves while cost is reduced.*

**27. Lack of post-discectomy adhesions following application of Adcon-L: a caes report.**

de Tribolet N, Robertson JT.

Service de Neurochirurgie, CHU Vaudois, Lausanne, Switzerland.

Eur Spine J **1996** ; 5 Suppl 1 :S18-20

*Summary : re-operation for reherniation in two patients, one treated with and one without Adcon-L at the primary surgery: extensive peridural adhesions in 1<sup>st</sup> patient, no scar or adhesions in 2<sup>nd</sup>.*

**28. Use of Adcon-L to inhibit post-operative peridural fibrosis and related symptoms during lumbar disc surgery: a preliminary report.**

Petrie JL, Ross JS.

Gliatech Inc., Cleveland, OH, USA.

Eur Spine J **1996** ; 5 Suppl 1 : S10-7

*Summary: prospective, randomised, multicenter, double-blind study in primary lumbar surgery: 23% reduction in number of patients with extensive scar, 120% increase in number withy minimal or no scar, 50% reduction of activity related pain.*