

# Albumin therapy enhances collateral perfusion after laser-induced middle cerebral artery branch occlusion: a laser speckle contrast flow study

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# Albumin

## Human serum Albumin (HSA) – Preparation

- extraction from a **plasma pool** via alcoholic precipitation
- **viurs inactivation** (pasteurization at +60°C for 10h)
- administration **independent of blood group** (no isoagglutinine)
- **isooncotic** (4-5%) or **hyperoncotic** (20-25%) solution
- exogen added albumin (natural or recombinant) inhibits endogen albumin synthesis



# Methods



**BALB/c  
mice**

**CD-1  
mice**

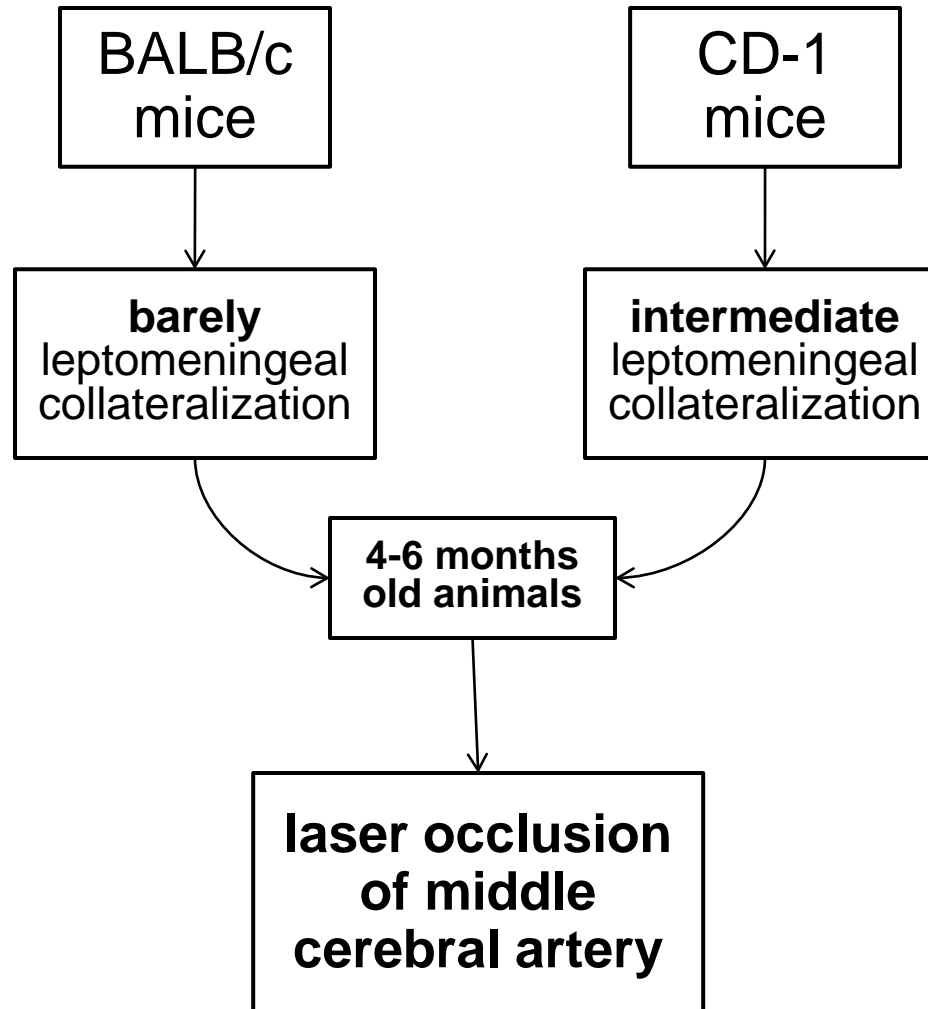


**barely  
leptomeningeal  
collateralization**

**intermediate  
leptomeningeal  
collateralization**

**4-6 months  
old animals**

**laser occlusion  
of middle  
cerebral artery**



# Methods

## Anesthesia

- 2% isoflurane via nose cone

## Monitoring

- rectal temperature
- arterial and venous catheter for blood gas analysis
- M. temporalis temperature via needle

## Scalp thinning with a carbide ball bit over the MCA

## Laser occlusion system

- described by *DeFazio* 2011
- „non-invasive“ – „less-invasive“ procedure
- the largest MCA branch was occluded
- occlusion was verified by the visible white clot and LSC imaging

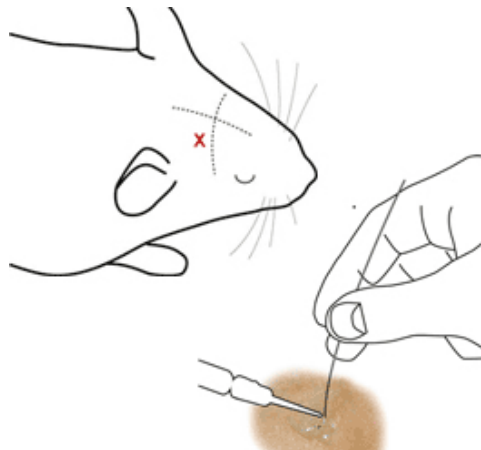
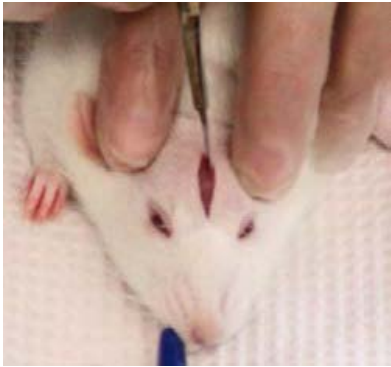
# Methods

- i.v. administered fluorescence beats were used to precisely position the laser beam on the area of interest
- 100% of animals showed persistent occlusion at day 3 in LSC and visual inspection

## Laser spectral imaging

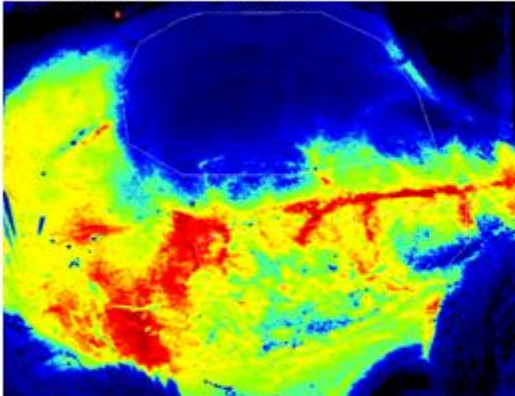
- an „image“ consist of 300 frames
- one image is generated in an 15s interval
- image analysis via ImageJ
- regions of interest were used to analyze changes in relative flow over time
- advantage: „non-invasive“ and continuous measurement over 90 minutes

# Methods

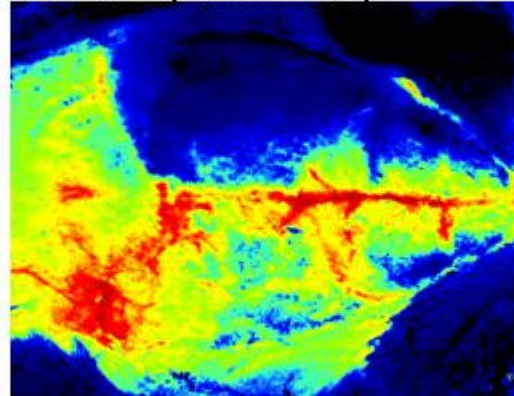


# Methods

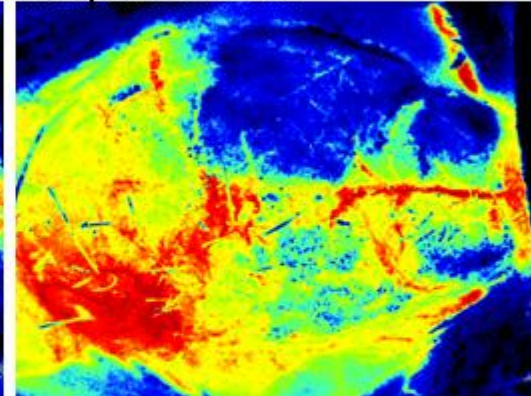
Induced stroke



Sham (Control)

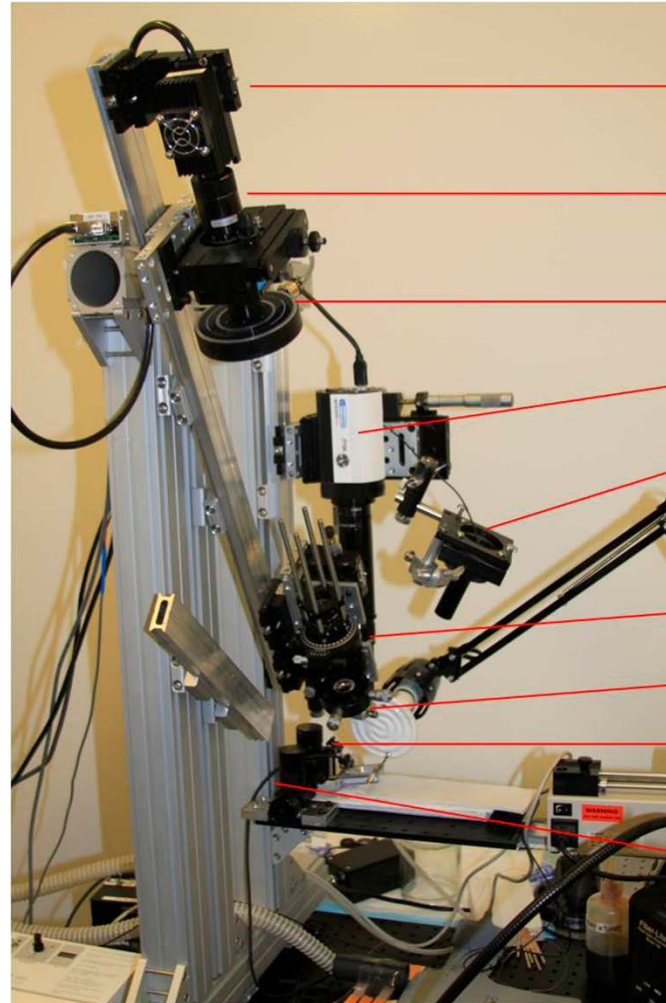


Reperfusion





# Methods



100 mW 532 nm DPSS laser

Beam telescope and positioner

Laser shutter

CCD camera to record  
laser speckle contrast

Laser-speckle illuminator

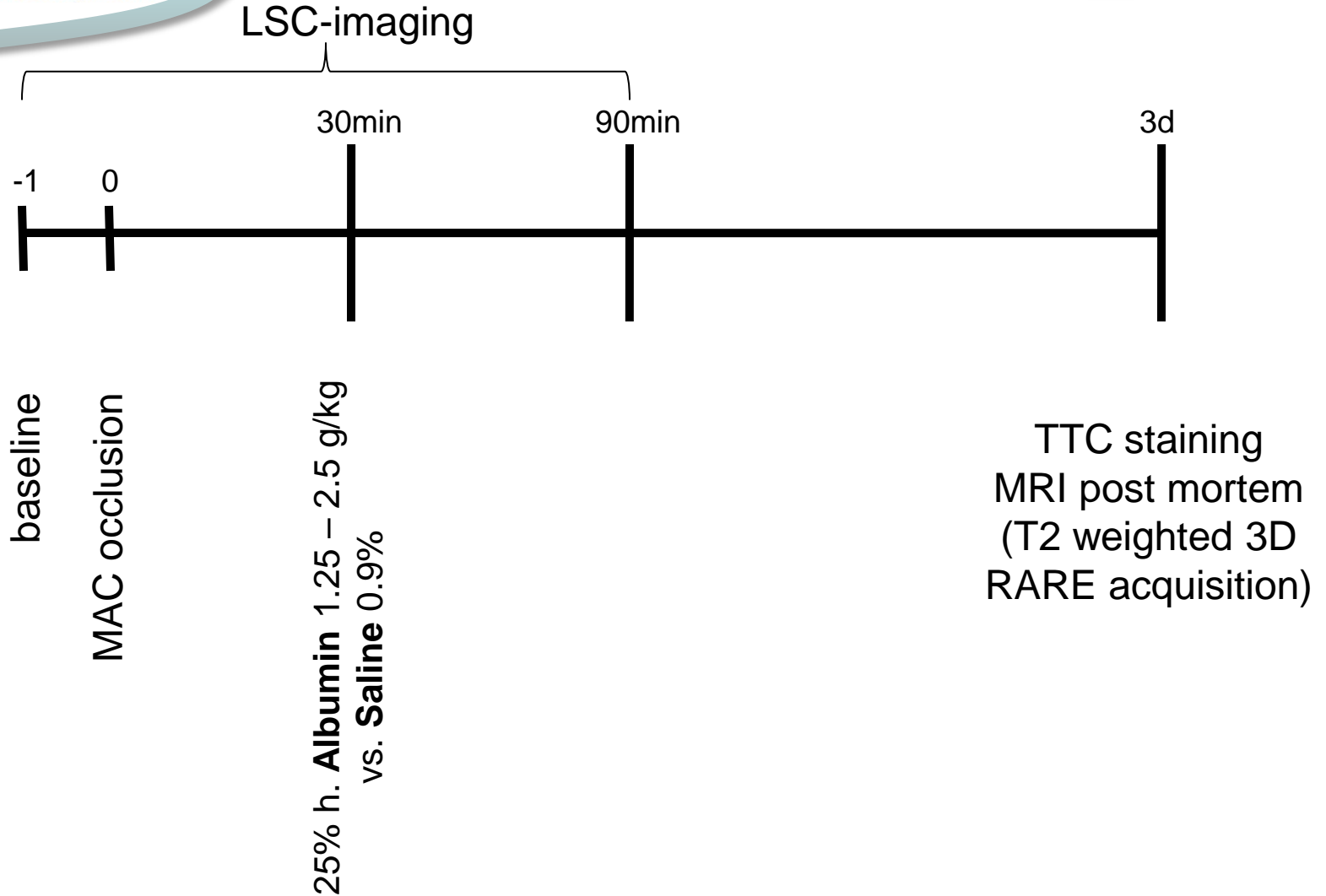
Crossed cylindrical lenses  
assembly

Beam positioner

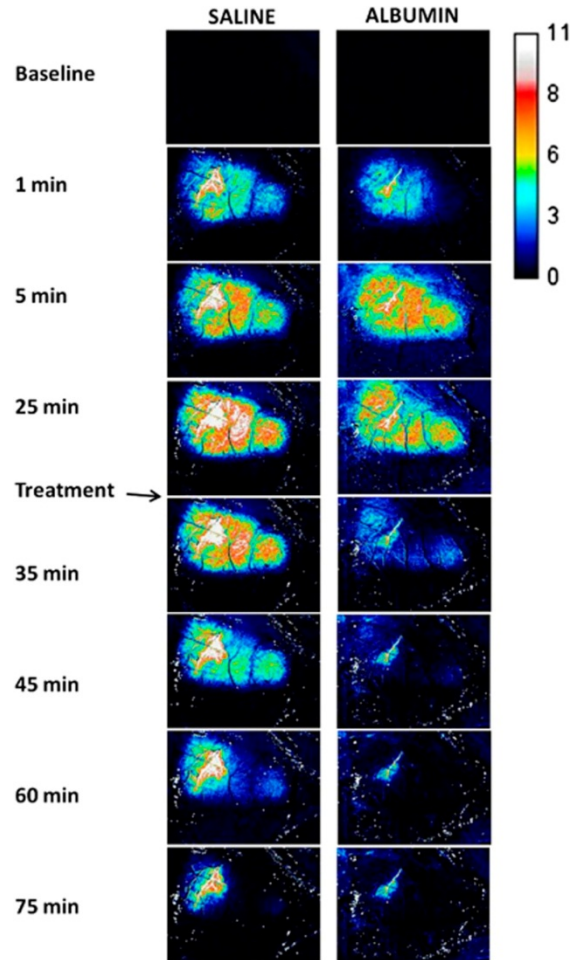
Infrared heating lamp

Mouse head holder  
and anesthesia,  
with XYZ-positioner





# Results



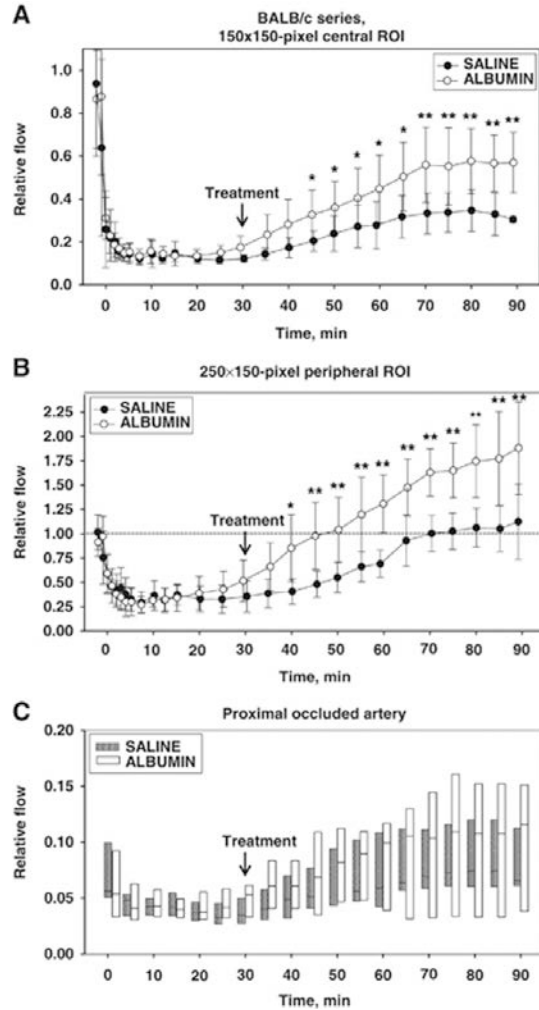
Laser-speckle inverse-flow difference images

# Results

„directly injured area“ →

penumbra →

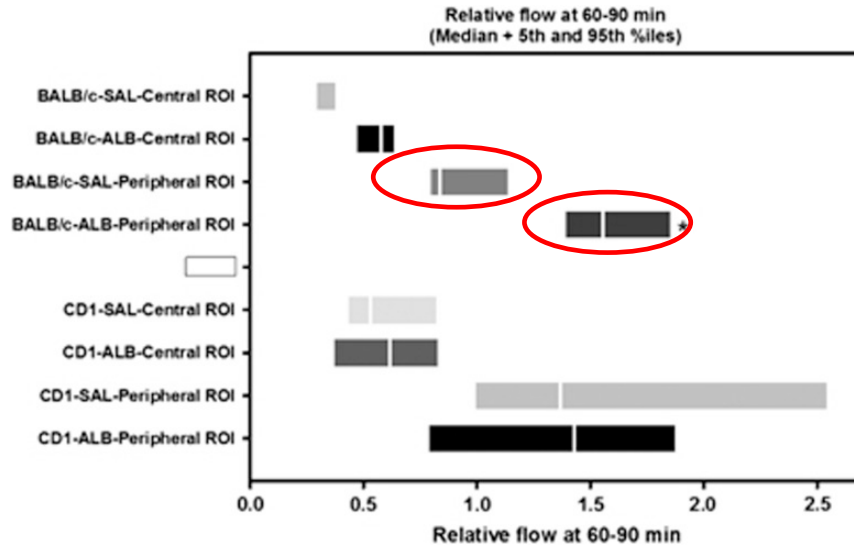
proximal occluded artery →



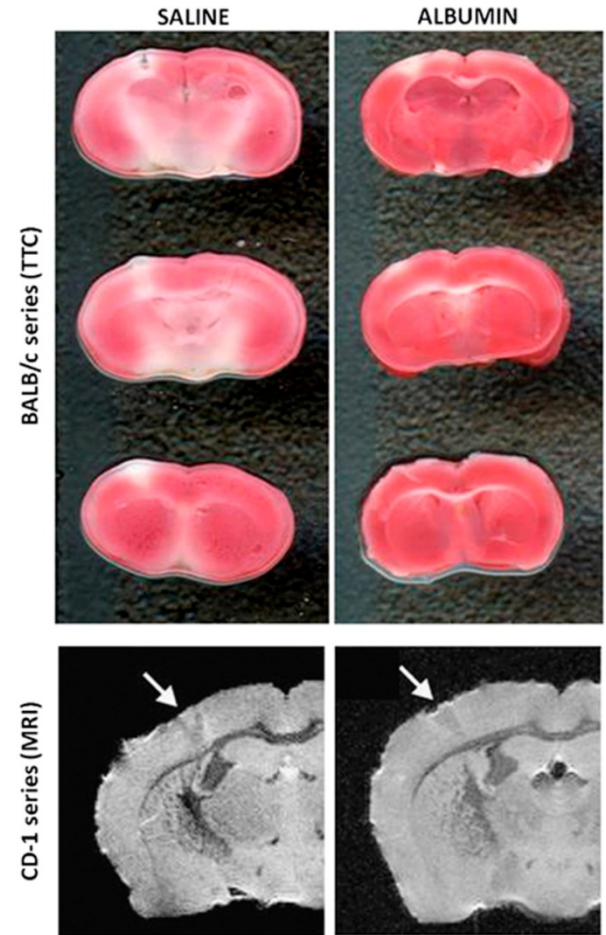
Time course of relative flow measured in the two ROI

# Results

Relative flow at 60 to 90 minutes after MCA branch occlusion in BALB/c and CD-1 mice

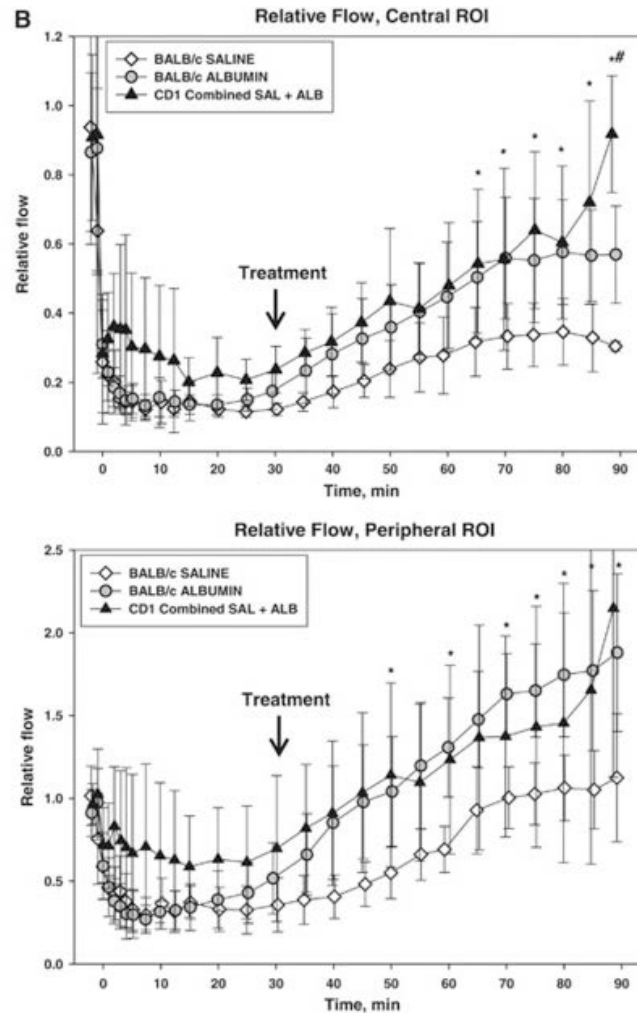


TTC-stained section showing the infarct in representative saline- and albumin-treated BALB/c mice



# Results

Relative flow (mean $\pm$ /-s.d.) shown separately for **saline-** and **albumin** treated **BALB/c** mice, and for combined **saline- plus albumin-** treated animals of the CD-1 series



# Discussion

1. **BALB/c** mice develop severe CBF reduction after MCA occlusion
2. **CD-1 mice**, which have an intermediate collateralization, do not develop an comparable stroke area
3. Albumin treatment did significantly improve CBF in the
  1. **central ROI** (the true stroke area) and
  2. **peripheral ROI** (=penumbra) in BALB/c mice



# Discussion

What might be an explanation?

- „**augmentation of collateral circulation**“ in BALB/c mice, while CD-1 mice did not evidence any positive effects
- platelet inhibition?
- Attenuate neutrophil extravasation
- modulation of vascular endothelial tone
- immune suppressive properties?<sub>1</sub>

# Excursus

*Controversial results on the effects of albumin administration to patients in the ICU have been reported.*

*Human Serum Albumin (HSA) solutions consist of **native HSA**, **degradation** products and **post-translational species** of HSA (i.e. nitrosylation, cyteinylation...)*

*It has been shown that commercial HSA products in vitro*

1. ***inhibit** PBMC stimulation*
2. ***inhibit** T-Lymphocyte activation*
3. *that the immune-modulatory component of **HSA is < 12.000 Da MW** as the dialyzed fraction (>12.000 da MW) failed to inhibit PBMC stimulation*

# Thank you for your attention