Vascular corrosion casting in cardiovascular research

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Abstract:
The increasing incidence of cardiovascular pathologies in Western community impels the use of animal models to examine human vascular disorders. Therefore, the present poster demonstrates some research applications of vascular corrosion casting in experimental animals.
In a first series of casts, wall shear stress (WSS), a major factor in the development of atherosclerosis and portal hypertension, was demonstrated in the mouse aortic arch (atherosclerosis) and the rat portal vein (portal hypertension). Batson's solution was injected into the abdominal aortas of healthy euthanized mice of various ages, and into the ileocolic veins of two rat models of portal hypertension, respectively. The first model was induced by a partial portal vein ligation (PPVL) mimicking portal vein thrombosis and resulting in the formation of collateral vessels. In the other model, secondary biliary cirrhosis and subsequent portal hypertension were obtained by a common bile duct ligation (CBDL). The macerated casts were scanned by micro-CT (computed tomography), computerized three dimensional (3D) reconstructions were made and a computational fluid dynamics (CFD) simulation was performed. CFD analysis showed a tendency towards lower WSS values in the larger aortic arches of older mice. This finding demonstrated the importance of accurately defining the animal model that is used. The CFD simulations differentiated PPVL rats from cirrhotic animals by the higher WSS values in the portal veins of the former. Moreover, a decrease of WSS in the portal vein together with an increase of WSS in

the collateral vessels correlated with a decompression of the portal vein by forming new blood vessels. A possible translation of these findings into the clinical domain is likely by the use of CFD analysis and non invasive diagnostic tools such as ultrasonic flow measurements and CT imaging. In addition, the CBDL model showed a capillary dilatation in the pulmonary arterial microcirculation, a hallmark feature of the hepatopulmonary syndrome.

In a second set of experiments, the vascular effects of blocking the angiogenic placental growth factor (PlGF) on mesenteric vessel formation was investigated in the mouse by scanning electron microscopy (SEM). The portal systems of euthanized PPVL mice were cast via the ileocolic vein. The results indicated that mice treated with antibodies against PlGF, experience a vascular regression which could be an effective strategy for reducing collateral vessel formation and lowering portal pressure.

In a last series of experiments, SEM was used to elucidate the angiogenic changes in a new mouse model of hepatocellular carcinoma. Vascular corrosion casts of livers were made by injecting Batson's solution into the abdominal aortas of mice having received intraperitoneal injections of the carcinogenic compound N-nitrosodiethylamine. The casts revealed chaotic patterns of hierarchically disorganized tumour induced blood vessels. Arterial mantles consisting of blood vessels showing both sprouting and intussusceptive angiogenesis ensheathed the tumours.

In general, it is concluded that vascular corrosion casting has recently revived as a research tool in the field of cardiovascular disorders. This technique is no longer exclusively used in descriptive anatomy, but has made its entry into experimental research. Together with SEM and micro-CT combined with 3D reconstruction it allows in-depth examination of the microcirculation or hemorheology.

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Vascular corrosion casting in cardiovascular research

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Introduction

The increasing incidence of cardiovascular pathologies in Western community impels the use of animal models to examine various human vascular disorders. Therefore, the present poster demonstrates some research applications of vascular corrosion casting in experimental animals.

Research applications of vascular corrosion casting

Wall shear stress determination

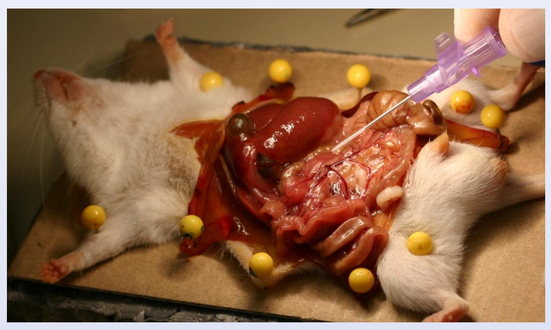

Fig. 1: Vascular casting of a mouse.

Wall shear stress (WSS), a major factor in the development of atherosclerosis and portal hypertension, was demonstrated in the **mouse aortic arch** (atherosclerosis) and the **rat portal vein** (portal hypertension). Batson's solution was injected into the abdominal aortas of mice, and into the ileocolic veins of two rat models of portal hypertension (Fig. 1). The first model was induced by partial portal vein ligation (PPVL), mimicking portal vein thrombosis. In the other model, secondary biliary cirrhosis and subsequent portal hypertension were obtained by common bile duct ligation (CBDL). Macerated casts were scanned by micro-CT (Fig. 2), followed by computerized 3D reconstructions and computational fluid dynamics (CFD) simulations.

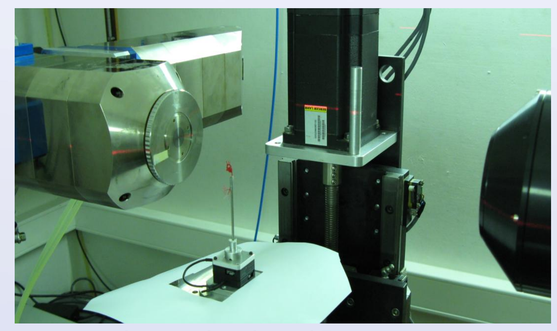

Fig. 2: In-house developed micro-CT system.

Mouse aortic arch: CFD analysis showed a tendency towards lower WSS values in the larger aortic arches of older mice (Fig. 3). This finding demonstrated the importance of accurately defining the animal model that is used. In particular, animal specific geometries and boundary conditions should be used.

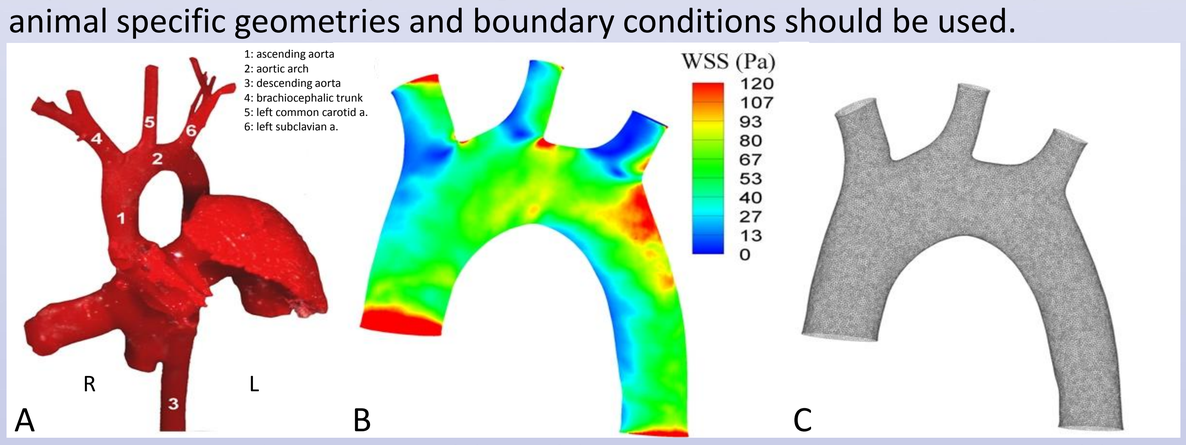

Fig. 3: Vascular cast of a murine aorta (A). WSS (B) can be calculated after micro-CT scanning (C).

Rat portal vein: CFD simulations differentiated PPVL rats from cirrhotic animals by higher WSS values in the portal veins of the former. A decrease of WSS in the portal vein together with an increase of WSS in collateral vessels correlated with a decompression of the portal vein by neo-angiogenesis (Fig. 4).

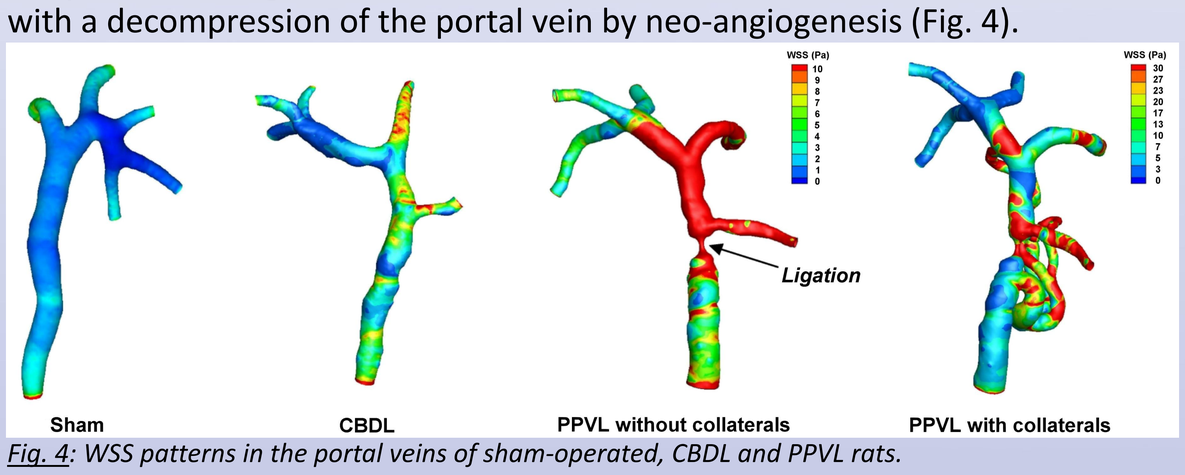

Fig. 4: WSS patterns in the portal veins of sham-operated, CBDL and PPVL rats.

Vascular effects of blocking angiogenic placental growth factor

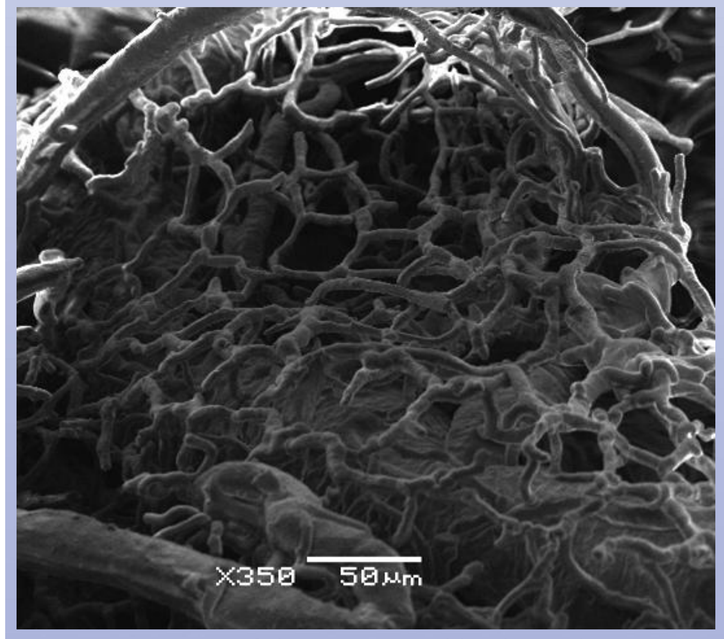

Fig. 6: SEM image of the mesenteric blood vessels in a PPVL mouse showing a dense network of capillaries.

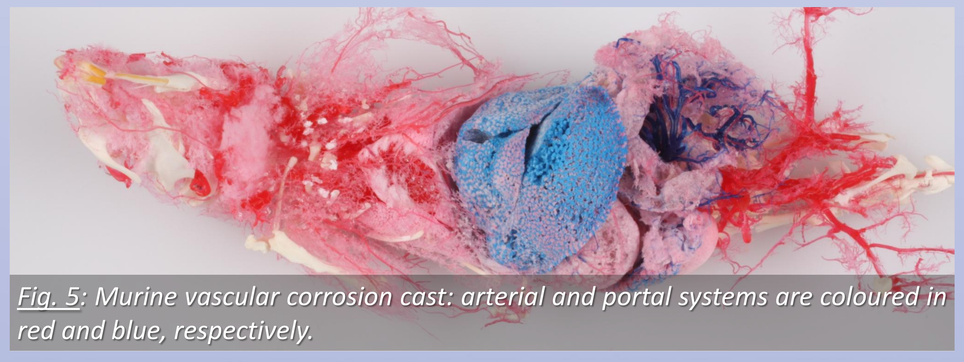

Fig. 5: Murine vascular corrosion cast: arterial and portal systems are coloured in red and blue, respectively.

The vascular effects of blocking the angiogenic placental growth factor (PlGF) on mesenteric vessel formation was investigated in the mouse by scanning electron microscopy (SEM). The portal systems of PPVL mice were cast via the ileocolic vein (Figs. 2, 5 and 6). The results indicated vascular regression in mice treated with antibodies against PlGF. This could be an effective strategy for reducing collateral vessel formation and lowering portal pressure (Fig. 7).

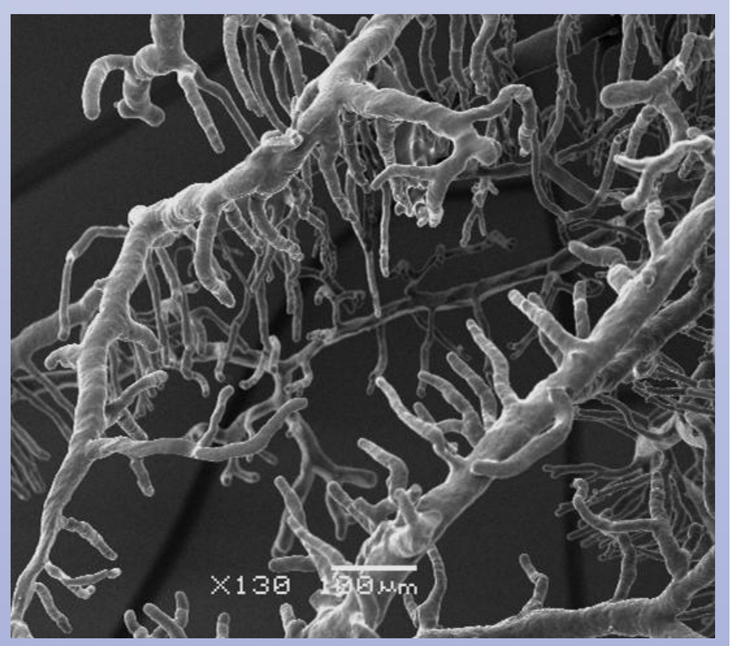

Fig. 7: Regression of the mesenteric blood vessels in a PPVL mouse treated with antibodies against PlGF (SEM image).

Angiogenic changes in a mouse model of hepatocellular carcinoma

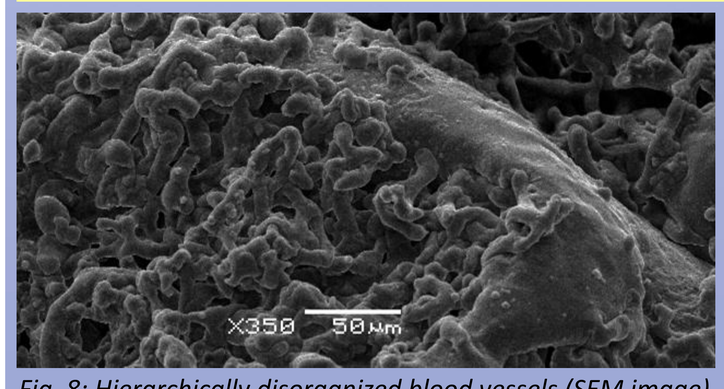

Fig. 8: Hierarchically disorganized blood vessels (SEM image).

SEM was used to elucidate the angiogenic changes in a new mouse model of hepatocellular carcinoma. Arterial corrosion casts of livers were made by injecting Batson's solution into the abdominal aortas of mice having received intraperitoneal injections of the carcinogenic compound N-nitroso-diethylamine. The casts revealed chaotic patterns of hierarchically disorganized tumour-associated blood vessels (Fig. 8). Arterial mantles consisting of blood vessels showing both sprouting and intussusceptive angiogenesis ensheathed the tumours (Fig. 9).

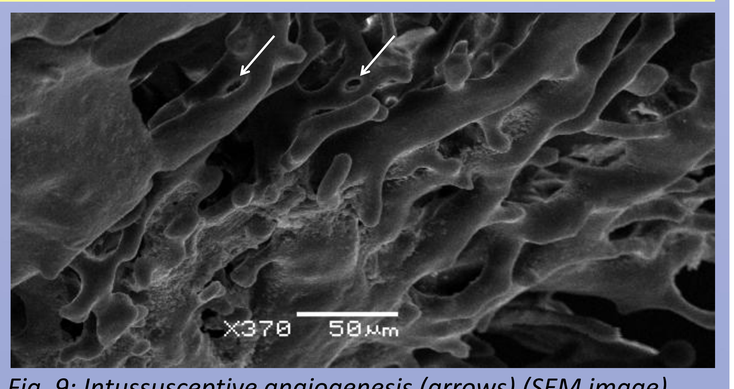

Fig. 9: Intussusceptive angiogenesis (arrows) (SEM image).

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