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EFFECT OF AGEING ON ELASTIN FUNCTIONALITY IN HUMAN CEREBRAL ARTERIES

E. Fonck (1, 5), G. G. Feigl (2), J. Fasel (3), D. Sage (4), M. Unser (4), D.A.Rüfenacht (5) & N. Stergiopulos (1)

Laboratory of Hemodynamics and Cardiovascular Technology, School of Engineering, Swiss Federal Institute of Technology,

Institute of Anatomy, Medical University of Graz, Austria.

Division of Anatomy, Department of Morphology, CMU Geneva, Switzerland.

Biomedical Imaging Group, Swiss Federal Institute of Technology, Lausanne, Switzerland.

Neuroradiology, Radiology Department, Geneva University Hospital, Switzerland.

BACKGROUND AND PURPOSE

The ageing process affects elastin, a key component of the arterial wall integrity and functionality. Elastin may play an important role in cerebral vessels because elastin degradation is linked to cerebrovascular disease [1]. The goal of this study is to assess the biomechanical properties of human cerebral arteries, their composition and geometry, with particular focus on the functional alterations of elastin in cerebral arteries due to ageing.

METHODS

12 segments of Left Posterior Cranial Arteries (PCAL) of two different age groups (mean age of the young group 42.2 years old; mean age of the old group 70.3 years old) were compared morphologically and were tested biomechanically before and after enzymatic degradation of elastin. Light and confocal microscope imaging were used to analyze and determine structural differences, potentially attributed to ageing. Elastin natural auto-fluorescence was used to qualitatively measure the degree of fibers alignment in the circumferential direction. The measurement of elastin fibers orientation was carried out in ImageJ; with the plug-in that we developed called "OrientationJ" to calculate the coherency coefficient of the elastin fibers. The coherency coefficient is derived from the major and minor axe diameters of an ellipse aligned along the apparent direction of the fibers and is based on the structure tensor [2]. A coherency coefficient close to 1, representing geometrically a very slender ellipse indicates a strong coherent orientation of the local fibers. In the other hand, a coherency coefficient close to zero, representing geometrically a circle denotes no preferential orientation of the fibers.

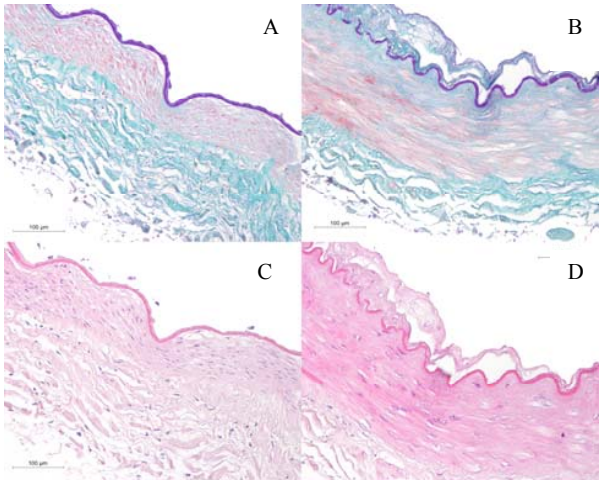

Figure 1. Histological sections of the posterior cerebral arterial wall of both young (A & C) and old (B & D) specimens stained with Aldhyde-Fuchsine (A & B) illustrating elastin fibers (purple), collagen fibers (green) and vascular smooth muscle cells (brown). Hemalun-Eosine staining (C & D) puts into evidence de VSMc nucleus (purple) and the matrix (pink).

RESULTS

Ageing has a significant impact on the structural morphology and on the mechanical properties of intracranial arteries [3, 4]. In contrast to main systemic arteries, intima and media thicken while outer

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diameter remains relatively constant with age, leading to concentric hypertrophy as shown in figure 1.

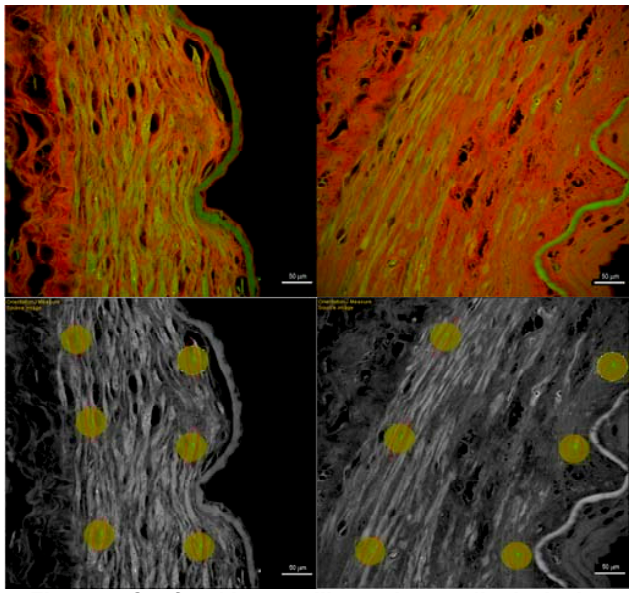

Figure 2. Confocal images illustrating qualitatively the orientation of elastin fibers for both young (A & C) and old specimens (B & D). Figures C and D show only the elastin matrix in the green channel from which coherency coefficients were calculated in the inner and outer media.

The structural morphology of elastin changed from a fiber network oriented primarily in the circumferential direction to a more heterogeneously oriented fiber mesh, especially at the intimal side (figure 2). The elastin fractional area ratio remains relatively constant between the two age groups, because the increase in collagen fiber area fraction is accompanied by a decrease in vascular smooth muscle cells. Biomechanically, cerebral arteries stiffen with age and lose compliance in the elastin dominated regime as shown in figure 3.

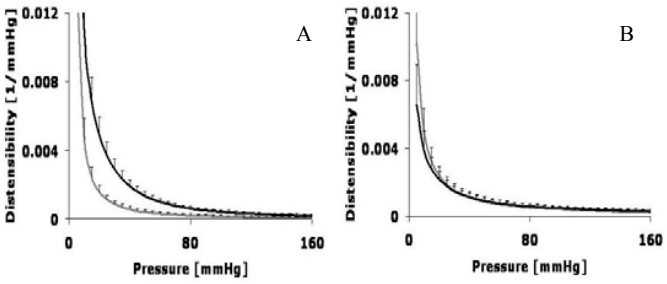

Figure 3. Pressure-distensibility curves of the control group (n=6) (black lines) and the elastase treated group (n=6) (gray lines) for both young (A) and old (B) groups.

Fragmentation of elastin by elastase treatment lead to loss in compliance and stiffening in the young group but did not significantly change either the structural or the material properties of the arteries in the older group, suggesting that elastin, though present in equal quantities in the old group, becomes dysfunctional with ageing.

DISCUSSION

The histological results showed that during ageing, the morphology and dimensions of the cerebral arteries change significantly and our findings are in agreement to the data reported by Hayashi et al.[4]. They also exhibit a more compact media and higher thickness to lumen diameter ratio than other cerebral arteries. We showed, through confocal microscopy a remarkable difference in the elastin structure in aged arteries as compared to young arteries. Indeed, the elastin of the young group is structurally organized in the circumferential direction whereas the elastin of the old group is distributed heterogeneously throughout the wall and lacks coherent orientation, primarily in the inner half of media. Also, the number of the elastin fiber increases with age and their density decreases. This change in fiber density could be the result of elastin fatigue as proposed by O'Rourke and Safar but most likely results from a differentiation of elastin fiber synthesis and its structural integration during ageing [5]. Destruction of the elastin by enzymatic elastase treatment of young human cerebral arteries significantly altered the biomechanical properties of the arterial wall as reflected on the distensibility. In contrast, degradation of elastic in aged human cerebral arteries did not markedly modify the biomechanical aspect of the arterial wall. At high pressures, collagen, which seemed to be unaffected by the elastase treatment limited arterial extension in a similar fashion in both control and treated arteries. These results, in conjunction with the fact that the fractional area of elastin in the old group is not different from the one in the young group, lead us to the conclusion that elastin is not reduced but becomes dysfunctional with ageing. Hence, once again, combined histological and biomechanical analysis has shown that the contribution of wall components to the biomechanical properties of the wall cannot be judged by histology alone. Structural integrity and integration are equally important factors.

CONCLUSIONS

Cerebral arteries remodel and adapt their geometry, elastic properties and function in the course of ageing. The loss of distensibility with ageing seems to be due to structural changes in the elastin fibers rather than loss in elastin content per se. It is noteworthy that elastin is present in both young and old age groups at equal fractional area levels. Elastin seems to be, however, non-functional in the old group, because its chemical disruption does not produce any significant change in the pressure-distensibility curve. Non-functional elastin and increased stiffness affects a number of biological functions on the arterial wall and may be implicated in various forms of cerebrovascular disease.

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