Liver changes in ageing

Liver volume/mass

methods: autopsy study, computerized tomography, radionucleotide scanning and ultrasonography

Liver volume	Study design	Reference
reduction of liver size in the order of 25-35%	Human, review	{Couteur1998}
-18% liver volume women [20 - 80] **-24%** liver volume man [20 - 80] most marked changes after 6th decade	Human, N=1582, age 20 - 80, autopsy after acute injury or accident	{Woodhouse1990} -> [71]
- **25% liver weight** [20-70] marked reduction in the elderly with -46% between 3rd and 10th decade	Human, autopsy study, age 20 - 70	{Woodhouse1990} -> [72]
1303ml (young) **990ml** (aged) **-24% liver volume**	human, ultrasonography, N=15 (third decade), N=11 (75-86 years)	{Woodhouse1990} -> [81 Swift1978]
significant negative correlation liver volume ~ age 1474ml (24 years) 934ml (91 years) **-37% liver volume (all)** **-44% liver volume (women)** **- 28% liver volume (men)**	human, ultrasonography, N=65, 24-91 years	{Woodhouse1990} -> [80 Wynne1989]
-33% liver volume (30-85 years)	human, ultrasonography	{Woodhouse1990} -> [84 Marchesini]

Liver blood flow

methods: clearance methods, echo Doppler

Liver blood flow	Study design	Reference
apparent blood flow falls with ageing	Human, Indocyanine green (ICG) clearance for apparent liver blood flow, N=20, 22-72years	{Woodhouse1990} -> [89 Wood1979, PMID: 445957]

-35% apparent liver blood flow (in >65 years vs. <40) **-11% perfusion** (in this age range)	Human, Indocyanine green (ICG) clearance for apparent liver blood flow, N=65, 24-91years	{Woodhouse1990} -> [80 Wynne1989]
total (THF) and functional (FHF) hepatic blood flow decrease in parallel with ageing **THF = 1445 +- 220 ml/min (<45years) to 1020 +-148 (>75years); P<0.001** **FHF = 1514 +- 250 ml/min (<45years) to 1015 +-163 (>75years); P<0.001** => with ageing there is a reduction of hepatic blood blow without any additional intrahepatic shunting	Human, N=40 normal total hepatic flow (THF) was measured by pulsed echo-Doppler (sum of portal and hepatic artery blood flow) functional hepatic flow (FHF) was measured by the hepatic clearance of D-sorbitol	{Anantharaju2002} -> Zoli1999
substantial reduction in blood flow of about 40% **Hepatic arterial supply as a proportion of cardiac output is constant and there are no major changes in portal venous haemodynamics with age**	review, documented in humans and rodents using a variety of techniques including dye clearance, indicator distribution and portal Doppler-ultrasound	{Couteur1998} - >[23-26, 33-35]

Sinusoidal blood flow

methods: high resolution fluorescence microscopy

Sinusoidal blood flow	Study design	Reference
decrease in sinusoidal blood flow velocity **222 +-24 µm/s (SEM) 12 month (rat)** **196+-22 µm/s (SEM) 24 month (rat)** **-12%** **decrease in sinusoidal blood flow** **7.8+-0.8 pL/s (SEM) 12 month (rat)** **6.8+-0.7 pL/s (SEM) 24 month (rat)** **perfusion rate of sinusoids unaltered around 100%** **99.6% 12 month (rat)** **98.4% 24 month (rat)**	Spraque-Dawley rats: life cylce ~30months, animals at th eage of 3months and 12months can be considered as young and mature, while 24month are senescent individuals	{Vollmar2002}

Morphological changes sinusoid

methods: high resolution fluorescence microscopy

Sinusoidal morphology	Study design	Reference
Increase in postsinusoidal venules size under constant sinusoidal density and diameter **venules length:** **349+-15 µm (SEM) 12 month (rat)** **445+-50 µm (SEM) 24 month (rat)** **venules diameter:** **37+-1 µm (SEM) 12 month (rat)** **49+-3 µm (SEM) 24 month (rat)** **sinusoidal density:** **7.8+-0.1 n/200µm (SEM) 12 month (rat)** **7.5+-0.2 n/200µm (SEM) 24 month (rat)** **sinusoidal diameter:** **6.66+-0.17 µm (SEM) 12 month (rat)** **6.66+-0.12 µm (SEM) 24 month (rat)**	Spraque-Dawley rats: life cylce ~30months, animals at th eage of 3months and 12months can be considered as young and mature, while 24month are senescent individuals	{Vollmar2002}
In general, lobular morphology of the liver did not differ between the four groups of age studied inasmuch as the observed liver tissue clearly exhibited the polygonal network of capillary sinusoids with drainage of blood flow into central postsinusoidal venules. The present experiments show that neither during maturation nor during ageing and sencescence significant remodelling of the liver occurs.	Spraque-Dawley rats: life cylce ~30months, animals at th eage of 3months and 12months can be considered as young and mature, while 24month are senescent individuals	{Vollmar2002}
sinusoidal volume density (relative volume) unchanged **12-15% of total intralobular volume regardless of animal age**	Rat liver	{Schmucker2005} -> Schmucker1978
Pseudocapillarization	**Study design**	**Reference**
Age-related pseudocapillarization	human surgical and post-mortem specimens with immunohistochemistry and TEM	McLean2003

age was associated with increased peri-sinusoidal expression of von Willebrand's factor, collagen I, collagen IV, and staining with Masson's trichrome **age-related thickening of the sinusoidal endothelium** **165±17nm young** **222±11nm middle-age** **289±9nm older** **age-related loss of fenestraetions (p<0.001)** **7.7±0.7 per 10µm young** **3.6±0.5 per 10µm middle-age** **1.5±0.4 per 10µm older** **age-related deposition of basal lamina and collagen**		
60% thickening of the endothelial lining **80% decline in the number of endothelial cell fenestraetations with increasing age** (Similar age-related changes in baboon liver: +70% endothelial thickness with ageing -60% fenestrations with ageing	Human, surgical and post mortem samples of human liver	{Schmucker2005} -> McLean2003, Cogger2003

Morphological changes hepatocyte structure

methods:

Morphological	Study design	Reference
'brown atrophy' appearance (also seen in younger patients with malnutrition and cachexia) **accumulation of lipofuscin (ceroid) in hepatocytes** The brown appearance is secondary to the accumulation of pigmented waste products within hepatocytes. The major pigment is the 'wear and tear' substance, lipofuscin, which consists of the end products of lipid peroxidation in lysosomes.		{Anantharaju2002} {Couteur1998}

macrohepatocytes and **polyploidy** with increase in nuclei and nucleoli during aging especially around the terminal hepatic veins **+27% polyploidization** (86-92 vs. young)		{Anantharaju2002} -> [8,9]
matrical density and number of mitochondria are decreased with aging in rats & humans, but the integrity of the mitochondria and enzymatic activity may remain unchanged with ageing		
increase in volume and/or in the number of dense bodies (secondary lysosomes, residual bodies, lipofuscin)	human and rodent hepatocytes	{Schmucker2005} -> Schmucker2002