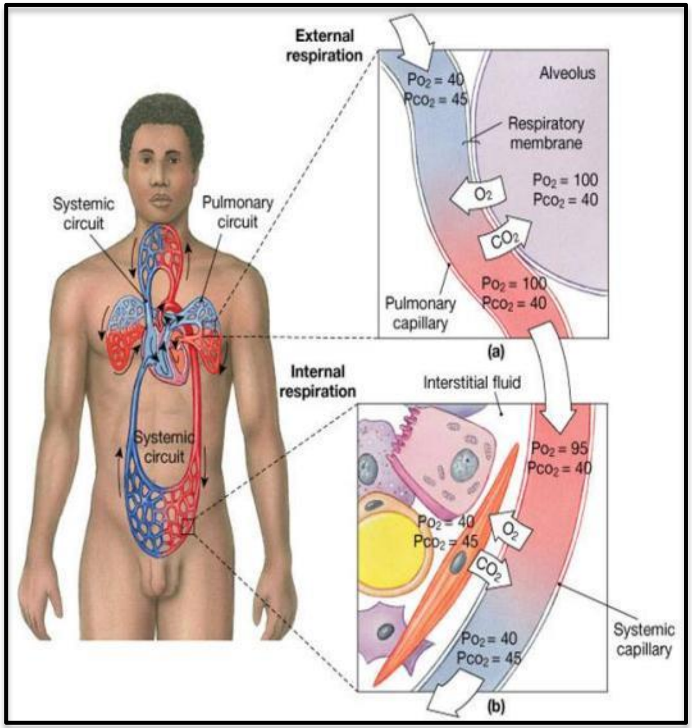
O_2 gradient in O_2 delivery system

Huaifa Zhang[1], Jake Barralet[1,2]

[1]Faculty of Dentistry, McGill University, Montreal, QC, H3A 0C7, Canada;

[2] Division of Orthopedics, Department of Surgery, Faculty of Medicine, McGill University, Montreal, QC, Canada

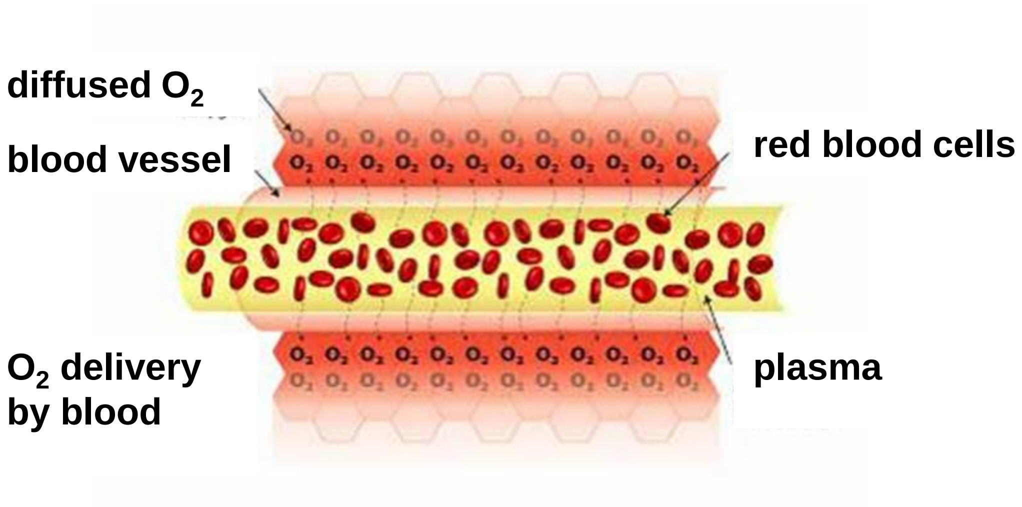
Respiration



Air is crucial for our life

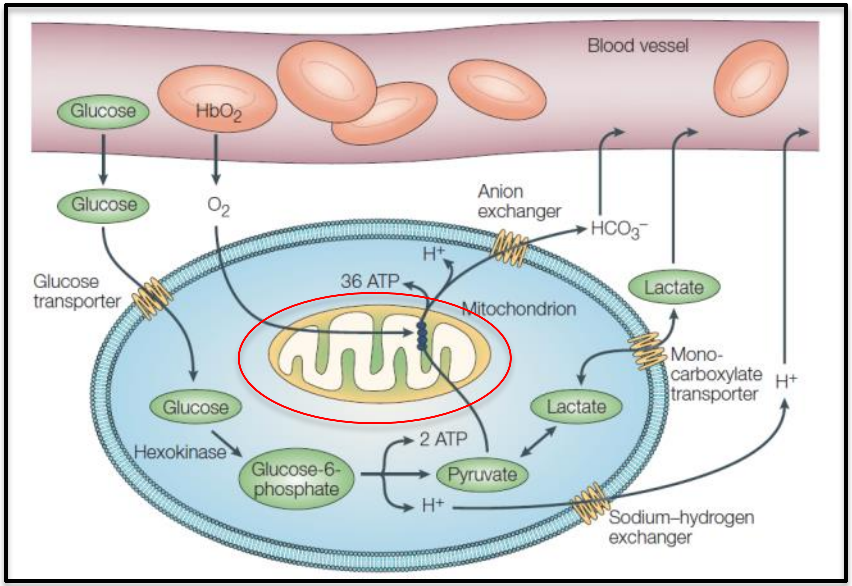
http://www.google.ca/imgres?imgurl=&imgrefurl=http%3A%2F%2Fwww.austincc.edu%2Fapreview%2FPhysText%2FRespiratory.html&h=0&w=0&tbnid=QW1I3bHxQkP7AM&zoom=1&tbnh=214&tbnw=235&doci

Tissue oxygenation



http://newleafhyperbarics.com/hyperbaric-oxygenation-effects-on-blood-flow/

Oxygen is crucial for cell activities



Role of O_2 in glucose metabolism in mammalian cells

Cell activities require energy, which mainly comes from the oxidative phosphorylation in mitochondria

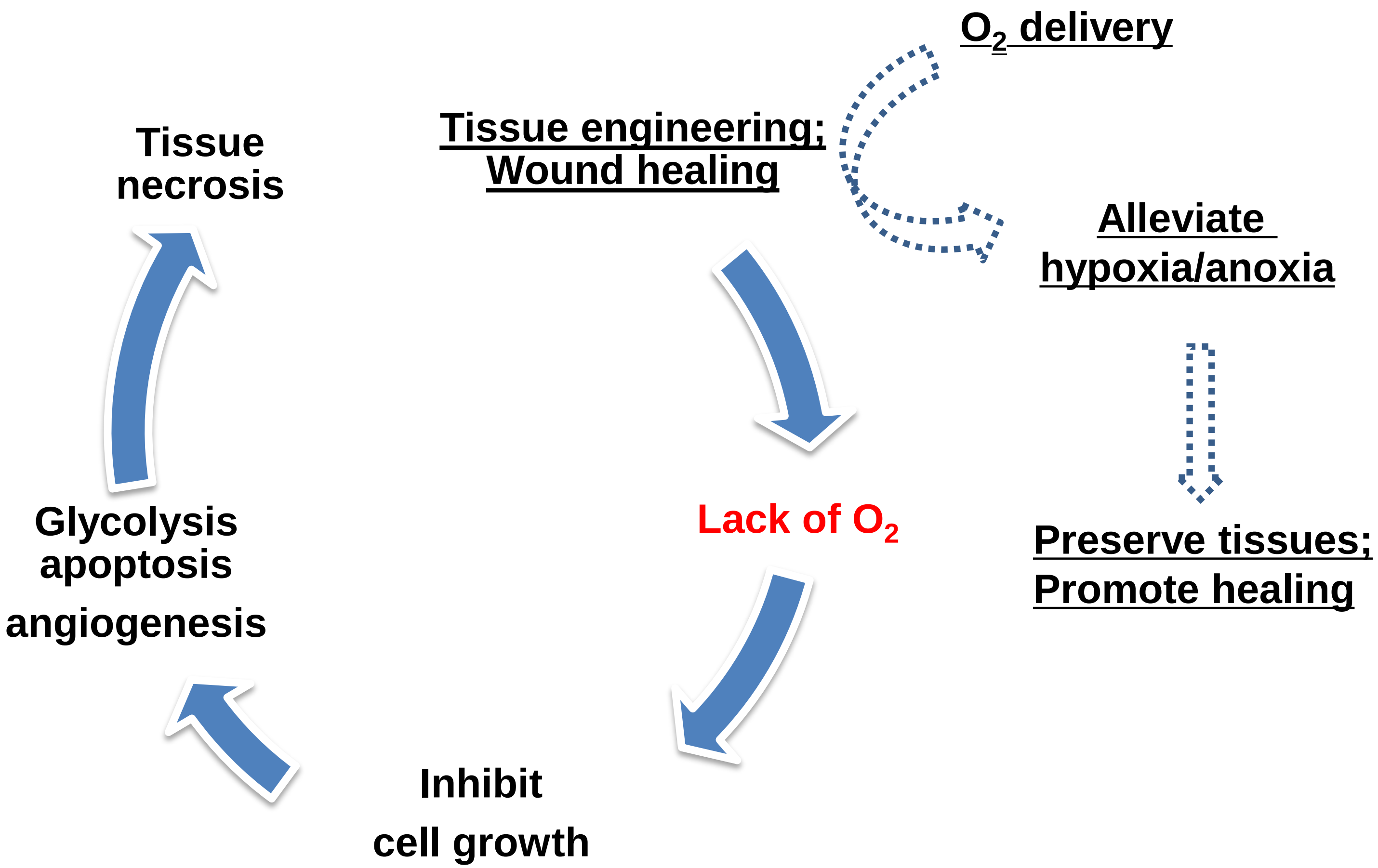
- **Oxidative phosphorylation can not take place without oxygen**
- **Lack of O_2 → lack of energy ⟶ metabolic crisis ⟶ cell death**

R. A. Gatenby and R. J. Gillies, *Nature Reviews Cancer*, 2004, 4, 891-899.

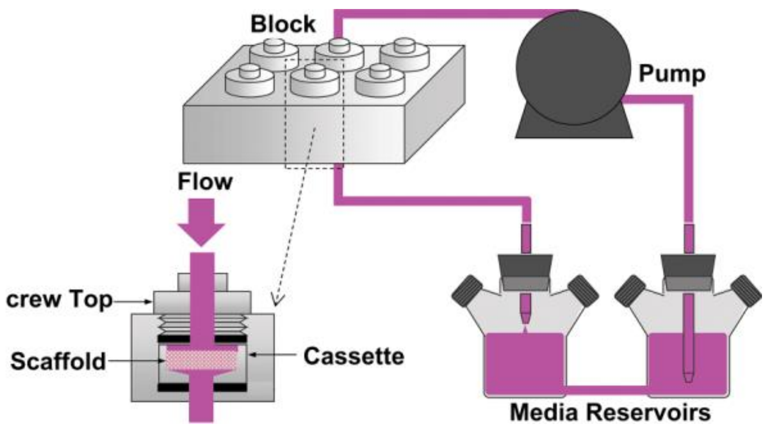
O_2 tension in tissues

	pO_2
Air	21.1%
Arterial blood	13.2%
Venous blood	5.3%
Cell	1.3-2.5%
Kidney	9.4%
Liver	5.4%
Muscle	3.8%

A. Carreau, B. E. Hafny-Rahbi, A. Matejuk, C. Grillon and C. Kieda, *Journal of cellular and molecular medicine*, 2011, 15, 1239-125

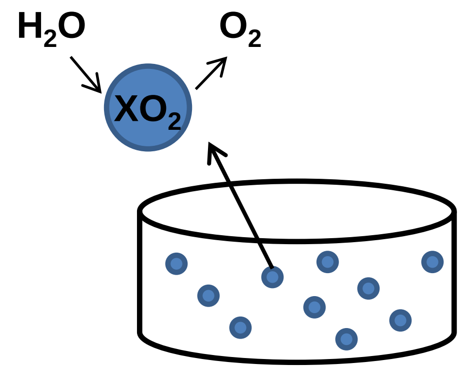

Tissue engineering; Wound healing
O_2 delivery
Alleviate hypoxia/anoxia
Preserve tissues; Promote healing
Lack of O_2
Inhibit cell growth
Glycolysis apoptosis angiogenesis
Tissue necrosis

Ways to deliver O_2



Perfusion bioreactor

Perfluorocarbons



O_2-generating scaffold

Kasper FK, http://www.stembook.org/node/478, 2008.

Riess, J.G. and M. Le Blanc, Pure Appl. Chem, 1982. 54(12): p. 2383-2406.

Harrison, B.S., et al., Biomaterials, 2007. 28(31): p. 4628-4634.

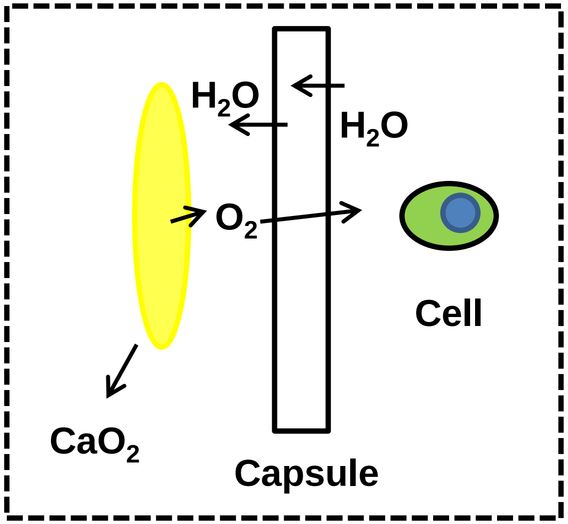
Basic Concept

Metal peroxide (CaO_2): O_2 generating agent

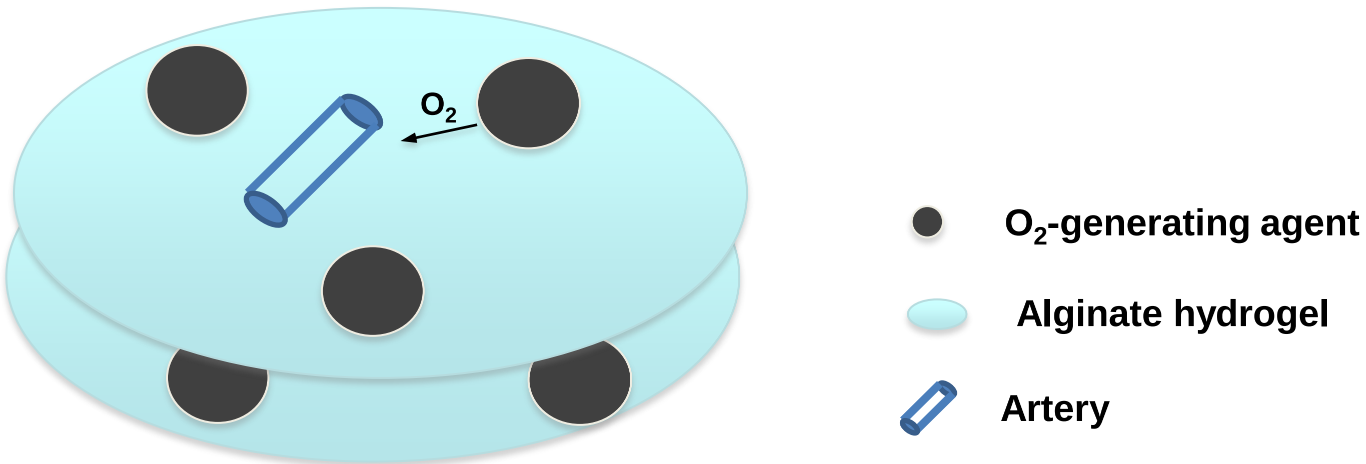
$$CaO_2 + 2\ H_2O = Ca(OH)_2 + H_2O_2$$

$$2H_2O_2 = 2H_2O + O_2\uparrow$$

Bioplymer capsule: control O_2 release



Self-oxygenating scaffold

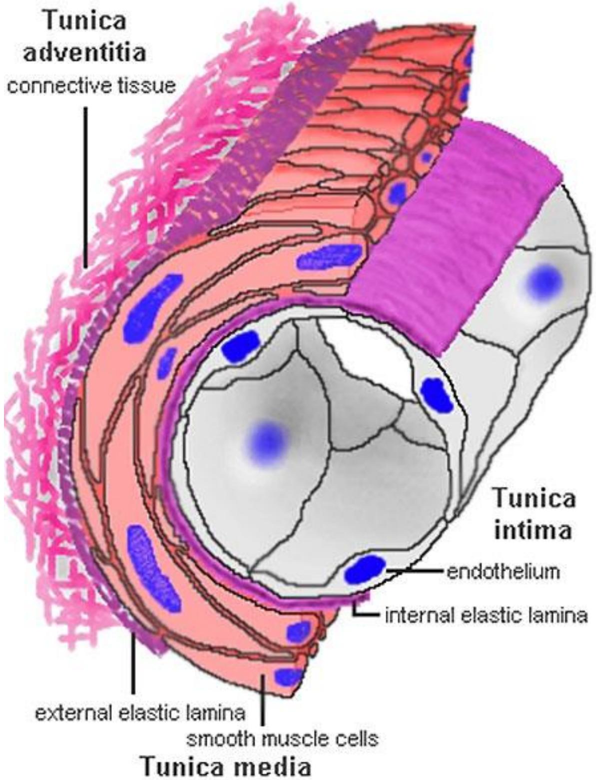


O_2-generating agent: CaO_2-polycaprolactone (PCL)

Blood vessel

Rat aorta size

Diameter (mm)	**2.24±0.07**
Wall thickness (mm)	**0.102±0.007**

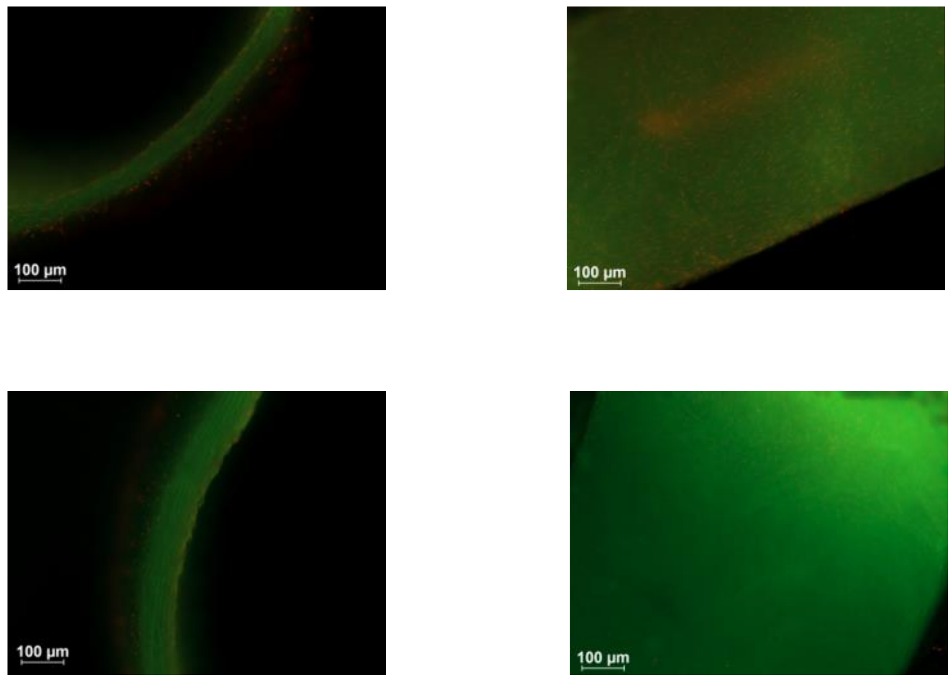


http://embryology.med.unsw.edu.au/embryology/index.php?title=HM_Practical_-_Blood_Vessel_Histology
H. WOLINSKY, *Circulation Research*, 1971, 28, 622-637.

Artery-cold storage

Decreasing temperature can reduce metabolic rate by 2-3 times every 10 ℃

	Cross section	Inner layer
Cold-7 d		
Cold+O_2-7 d		



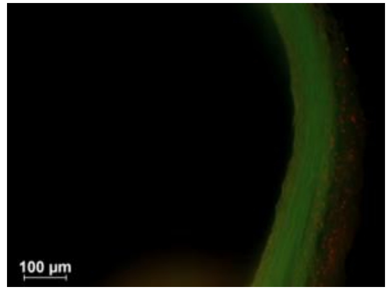
Green: live
Red: dead

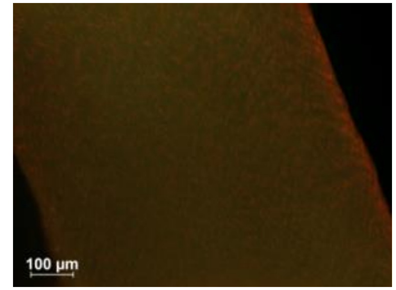
J. D. Litzgus and W. A. Hopkins, *Journal of Thermal Biology*, 2003, 28, 595-600.

Artery-normothermic storage

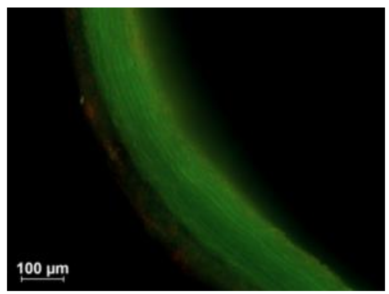
Cross section | **Inner layer**

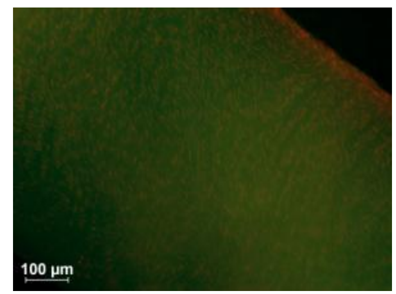
20% O_2-7 d



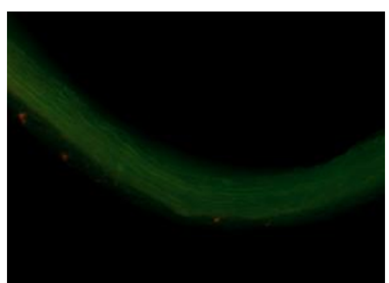


0% O_2-7 d

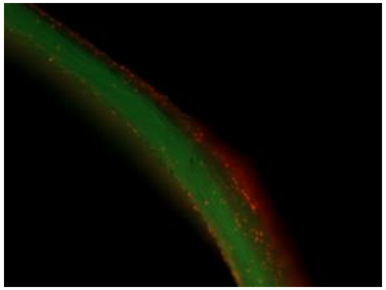
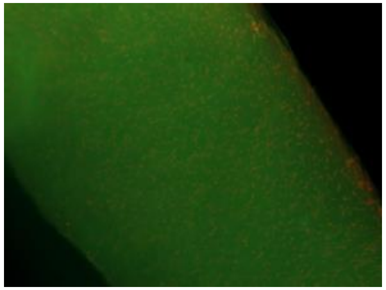
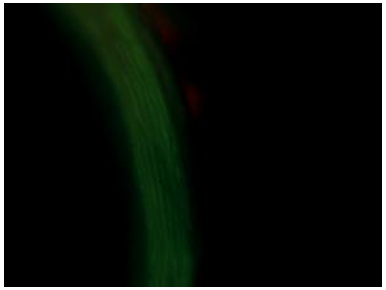
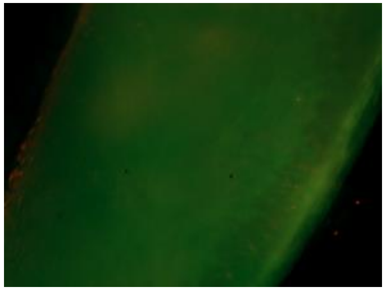
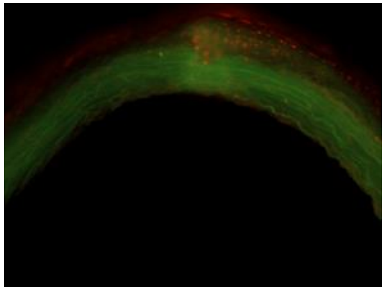
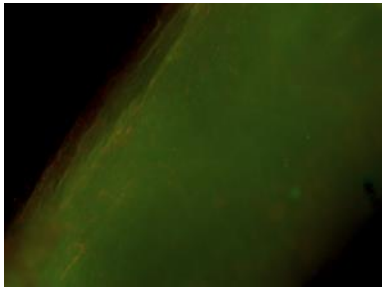




0% O_2+O_2-7 d



Artery-normothermic storage

	Cross section	Inner layer
0% O_2+O_2 (inside)-2 d		
0% O_2+O_2 (outside)-2 d		
0% O_2+O_2 (outside)-7 d		

Objective

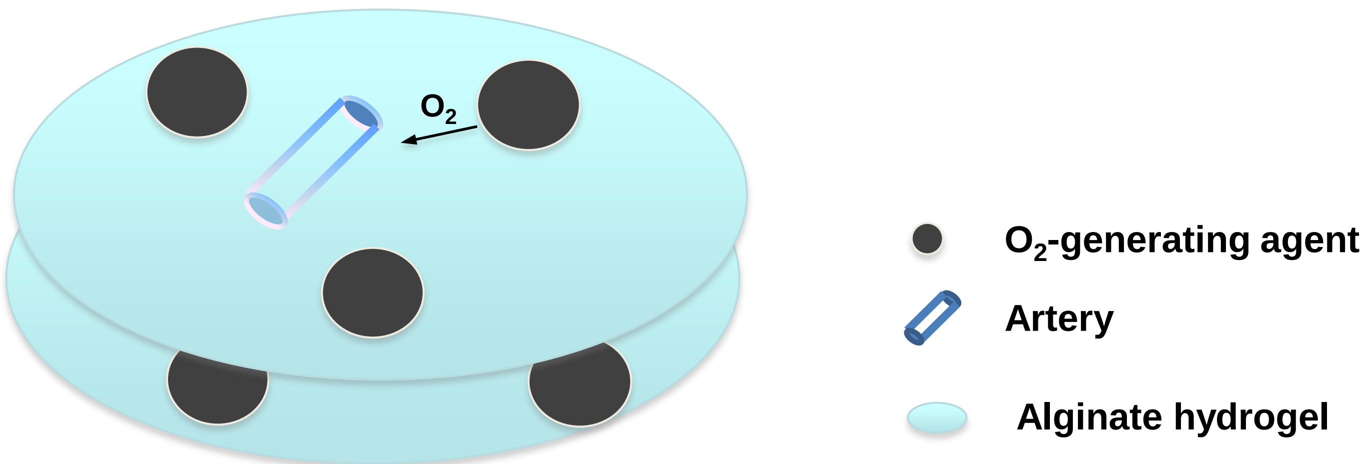
The process of O_2 transfer from O_2-generating agent towards aorta

Fick's law

$$J = -D\frac{\partial c}{\partial x}$$

J is the rate of transfer per unit of area ($\frac{g}{t \cdot cm^2}$); C the concentration of diffusing substance ($\frac{g}{cm^3}$); x the space coordinate measured normal to the section (cm); D the diffusion coefficient ($\frac{cm^2}{t}$).

O_2 delivery



Decomposition rate of CaO_2 (particle size, available amount of H_2O, precipitation of $Ca(OH)_2$)

Amount of generated O_2 (CaO_2 amount, decomposition rate)

O_2 diffusion rate in hydrogel, PCL, medium and artery (diffusion coefficient, O_2 gradient)

O_2 consumption (tissue mass, temperature)

M. Jamnongwong, K. Loubiere, N. Dietrich and G. Hébrard, *Chemical Engineering Journal*, 2010, 165, 758-768.
A. Axelsson, B. Persson, Applied biochemistry and biotechnology, 18 (1988) 231-250.

Decomposition rate of CaO_2

	CaO_2	CaO_2-PCL
Decomposition ratio (6 h)	**41.4% [1]**	**13.8% [2]**

[1] CaO_2 powders in 1% alginate hydrogel, 37 ℃, culture medium, by XRD data
[2] CaO_2 –PCL in 1% alginate hydrogel, 37 ℃, culture medium, by XRD data

J.-S. Yoon, H.-W. Jung, M.-N. Kim, E.-S. Park, Journal of Applied Polymer Science, 77 (2000) 1716-1722.
P. Das, D. Biswas, S. Roy, International Journal of Drug Delivery, 4 (2012) 20-30.

Diffusion coefficient of H_2O

	Hydrogel	PCL
Diffusion coefficient (cm^2/s)	$D = \pi R_0^2(k/4)^{1/n}$ [1]	22.9×10^{-8} [2]

Equilibrium H_2O content in PCL: 6.29×10^{-3} g/g of PCL

[1] D: diffusion coefficient of water ($cm^2\ min^{-1}$); R_0: radius of the dry gel; k: swelling constant; n: diffusional exponent (n = 0.45 indicates Fickian diffusion, $0.5<n<0.89$ indicates anomalous transport and $n\geq0.89$ implies relaxation-controlled transport). poly-acrylate

[2] 36.5 ℃, 0.072 atm H_2O vapor, Mn 23,200

J.-S. Yoon, H.-W. Jung, M.-N. Kim, E.-S. Park, Journal of Applied Polymer Science, 77 (2000) 1716-1722.
P. Das, D. Biswas, S. Roy, International Journal of Drug Delivery, 4 (2012) 20-30.

Diffusion coefficient of O_2

	1% calcium alginate	PCL	H_2O	Arteriolar wall	Tissues
Diffusion coefficient (cm^2/s)	1.75×10^{-9}	2.34×10^{5}	3.01×10^{-5}	$2.0 \pm 0.5 \times 10^{-6}$ [1]	$C - \frac{\alpha(Hx-x^2)}{2U}$ [2]

[1] *In vivo*, mouse
[2] C is the external O_2 tension, α is the respiration rate of the tissue, H is the slice thickness in cm and U is the O_2 tension at a point distance x cm inside the surface, a is the solubility of O_2 in the liquid

S. K. Young, et al, Polymer, 2002, 43, 6101-6114.
J. D. B. Macdougall and M. McCabe, Nature, 1967, 215, 1173-1174.
A.C. Hulst, et al, Biotechnol Tech, 3 (1989) 199-204.
N. Sasaki, et al, The Keio journal of medicine, 61 (2012) 57-65.

O_2 consumption rate

	Endothelial cells (suspension)	Smooth muscle cells	Arteriolar wall (*in vivo* mouse)
O_2 consumption rate (mol min^{-1} per cell)	$3.07\pm\times10^{-15}$ (mouse, 37 ℃) $0.61\pm0.32\times10^{-15}$ (pig, 4 ℃) $1.00\pm0.15\times10^{-15}$ (pig, 22 ℃)	$2.64\pm0.09\times10^{-15}$ (pig, 22 ℃)	5.71×10^{-5} ($mol\cdot100\ cm^{-3}\ tissue\cdot min^{-1}$)

O_2 consumption rate: around 3.0×10^{-15} mol min^{-1} per cell

R.P. Pandian, V. Kumar Kutala, N.L. Parinandi, J.L. Zweier, P. Kuppusamy, Archives of Biochemistry and Biophysics, 420 (2003) 169-175.
R. Motterlini, H. Kerger, C.J. Green, R.M. Winslow, M. Intaglietta, Depression of endothelial and smooth muscle cell oxygen consumption by endotoxin, 1998.

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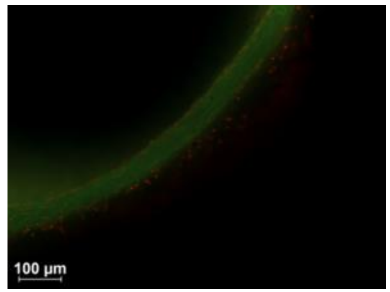
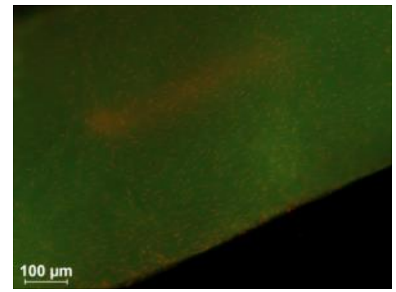
Artery-cold storage

Cross section

Inner layer

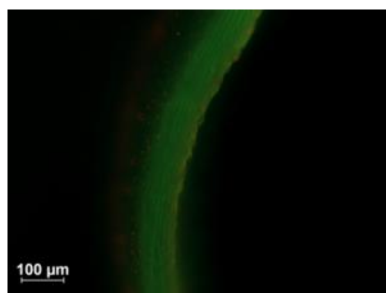
Cold-7 d

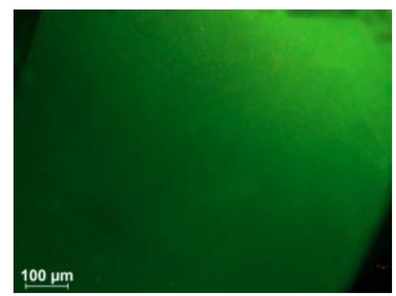




Cold+O_2-7 d

5 mg/ml particles in 1% gel

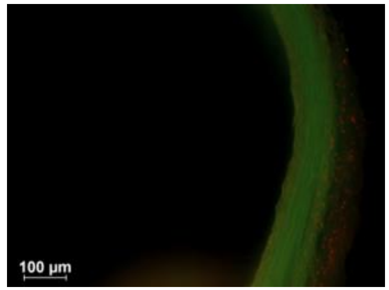


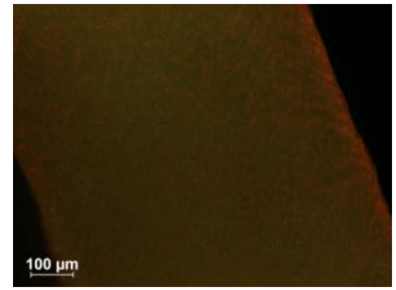


Artery-normothermic storage

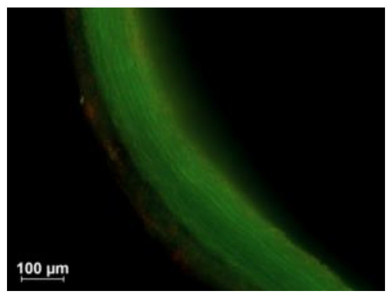
Cross section | **Inner layer**

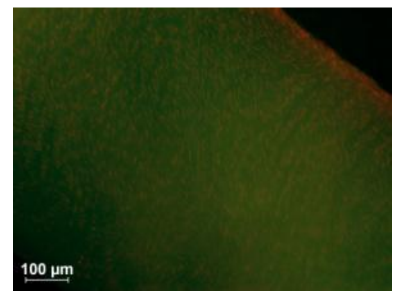
20% O_2-7 d





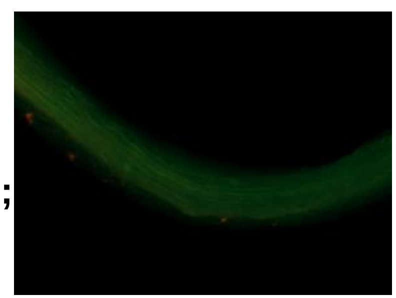
0% O_2-7 d

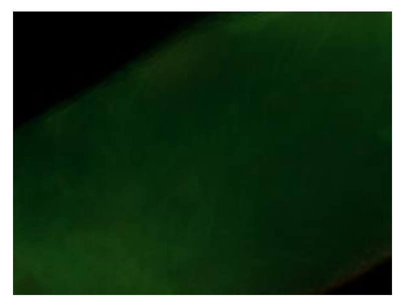




0% O_2+O_2-7 d

80 mg/ml particles in 1% gel; culture medium (DMEM)





Example model

2 D system simulation

$$\frac{\partial C_{oxy}}{\partial_t} = D\nabla^2 C_{oxy} + R_{oxy}$$

C_{oxy}: O_2 concentration, R_{oxy}: rate of O_2 production, D: diffusion coefficient of O_2

COMSOL software, Chemical Engineering Reaction module for fine element analysis (COMSOL 2010b; COMSOL 2010a) for CaO_2 decomposition in PDMS (R_{oxy})

E. Pedraza, M.M. Coronel, C.A. Fraker, C. Ricordi, C.L. Stabler, Proceedings of the National Academy of Sciences, 109 (2012) 4245-4250.

Solubility of O_2

	H_2O	PCL
Solubility (ppm)	6.73 ppm (37 ℃)	53.63 ppm (25 ℃)

S. K. Young, et al, Polymer, 2002, 43, 6101-6114.