Oxygenation of Blood by Photocatalytic Action

A.Subrahmanyam
Department of Physics
Indian Institute of Technology
Madras Chennai

Dr.T.Paul Ramesh
Apollo Hospital
Department Cardiothoracic Surgery
Apollo Hospitals
Chennai


CORSAIR
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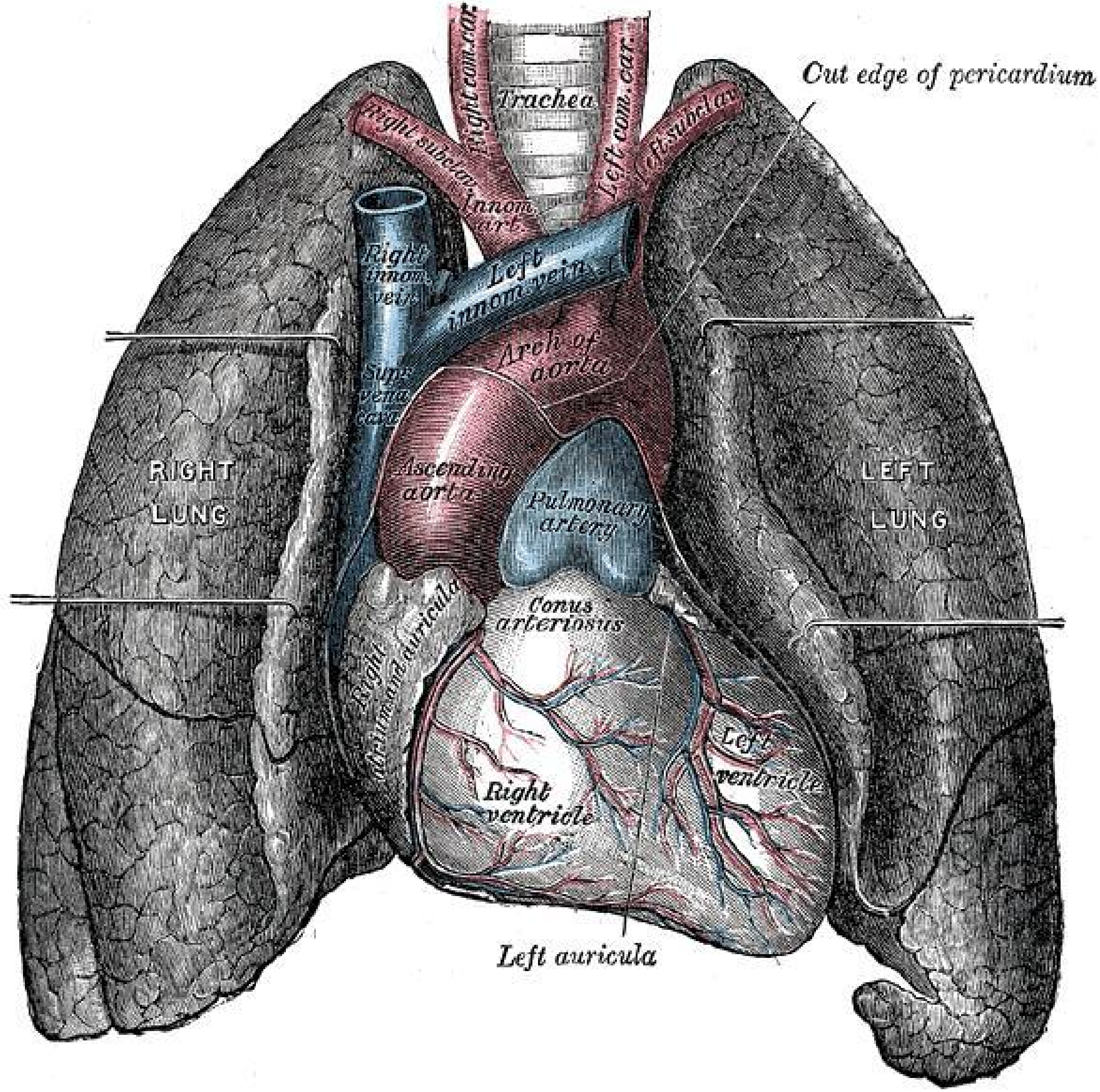
Why Oxygen?

Oxygen increase in atmosphere

- 2300 million years ago
- Photo dissociation

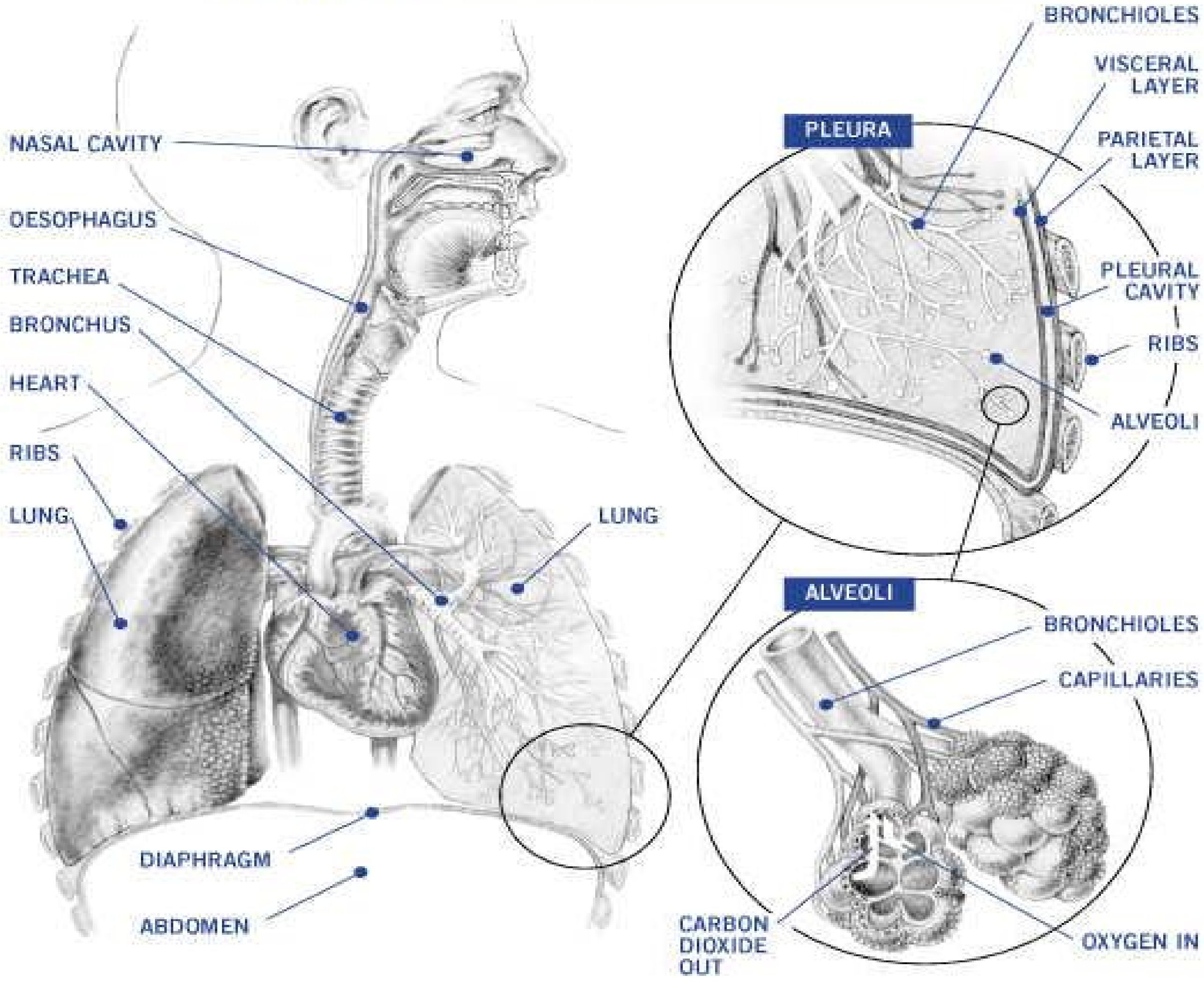
  $H_2O \xrightarrow{\text{UV Light}}$ Hydrogen + Oxygen
- 21% of present day atmosphere
- Most efficient at producing high-energy molecules like ATP (adenosine triphosphate)

How do lungs work?



Alveolar –capillary area ~ Tennis court surface (100-150 m²)

THE LUNGS



NASAL CAVITY
OESOPHAGUS
TRACHEA
BRONCHUS
HEART
RIBS
LUNG
LUNG
DIAPHRAGM
ABDOMEN
PLEURA
BRONCHIOLES
VISCERAL LAYER
PARIETAL LAYER
PLEURAL CAVITY
RIBS
ALVEOLI
ALVEOLI
BRONCHIOLES
CAPILLARIES
CARBON DIOXIDE OUT
OXYGEN IN

A little basics of Lungs, Blood and Red Blood cells

Normal blood gas values are as follows:

Partial pressure of oxygen (PaO_2): 75–100 mm Hg
Partial pressure of carbon dioxide ($PaCO_2$): 35–45 mm Hg
Oxygen content (O_2Ct): 15–23%
Oxygen saturation (SaO_2): 94–100%
Bicarbonate (HCO_3): 22–26 mEq/liter
pH: 7.35–7.45.

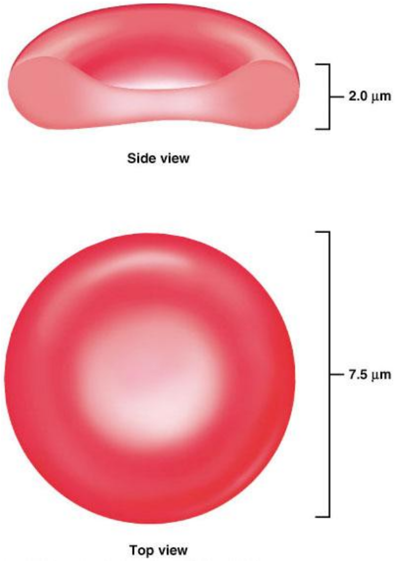
Composition of Blood

- **Blood is the body's only fluid tissue**
- **It is composed of liquid plasma and formed elements**
- **Formed elements include:**
  - **Erythrocytes, or red blood cells (RBCs)**
  - **Leukocytes, or white blood cells (WBCs)**
  - **Platelets**
- **Hematocrit – the percentage of RBCs out of the total blood volume**

- **Blood transports:**
  - **Oxygen from the lungs and nutrients from the digestive tract**
  - **Metabolic wastes from cells to the lungs and kidneys for elimination**
  - **Hormones from endocrine glands to target organs**

- **Blood maintains:**
  - **Appropriate body temperature by absorbing and distributing heat**
  - **Normal pH in body tissues using buffer systems**
  - **Adequate fluid volume in the circulatory system**

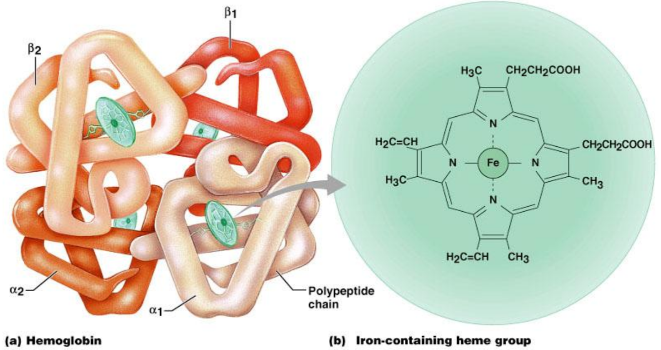
Every cell in human body requires Oxygen
The Oxygen is carried by the Blood

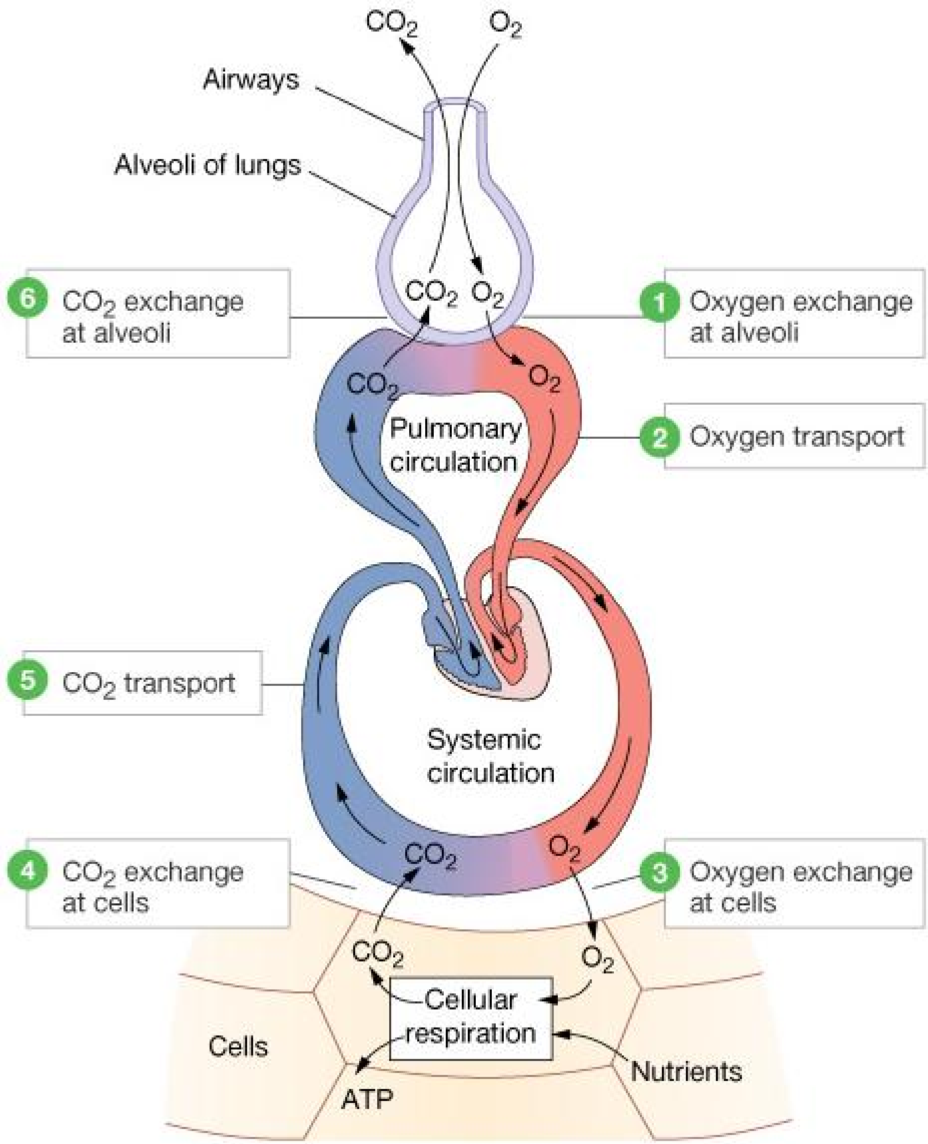


-Oxygen is carried in the blood in two forms.
-Most is carried combined with haemoglobin,
but there is a very small amount dissolved in the plasma.
-Each gram of haemoglobin can carry 1.31 ml of oxygen
when it is fully saturated.
-Every litre of blood with a Hb concentration of
15g/dl can carry about 200 mls of oxygen
when fully saturated (occupied) with oxygen
(PO2 >100 mmHg).

Functions of blood

1. Carry oxygen from lungs
2. Carry carbon dioxide to lungs
3. Carry nutrients from digestive system/storage
4. Carry wastes to liver/kidneys
5. Carry hormones to target cells
6. Carry heat to skin—body temp. regulation
7. Immune response—toxins, microorganisms
8. Clot blood—minimize nutrient loss
9. Water balance
10. pH balance--buffer





CO_2
O_2
Airways
Alveoli of lungs
CO_2 O_2
6 CO_2 exchange at alveoli
1 Oxygen exchange at alveoli
CO_2
O_2
Pulmonary circulation
2 Oxygen transport
5 CO_2 transport
Systemic circulation
CO_2
O_2
4 CO_2 exchange at cells
3 Oxygen exchange at cells
CO_2
O_2
Cellular respiration
Cells
Nutrients
ATP

Stepwise Reaction:

Hb + O2 <-> HbO2

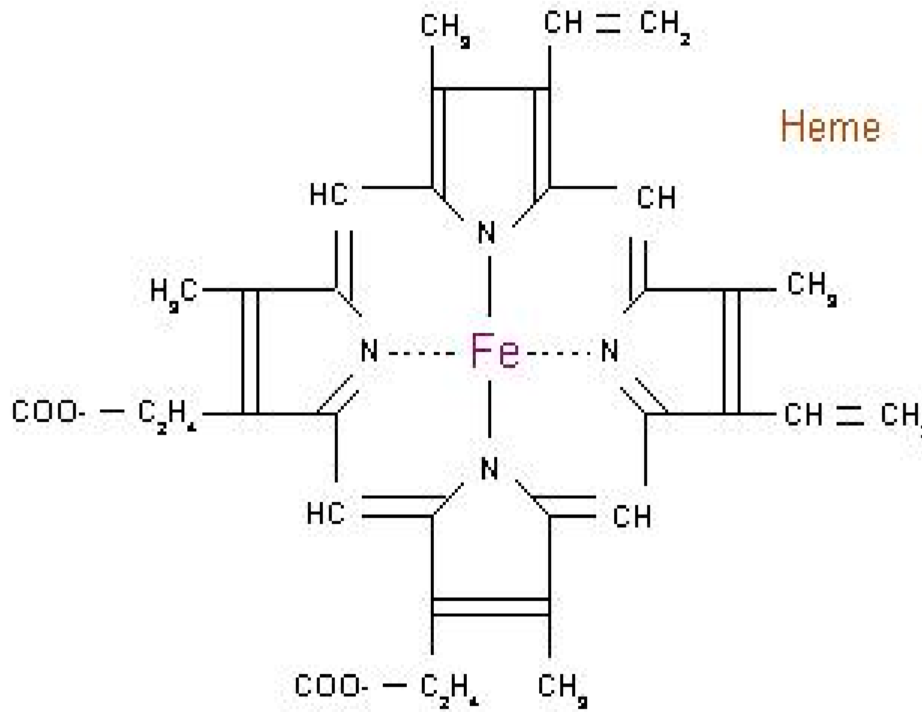
HbO2 + O2 <-> Hb(O2)2

Hb(O2)2 + O2 <-> Hb(O2)3

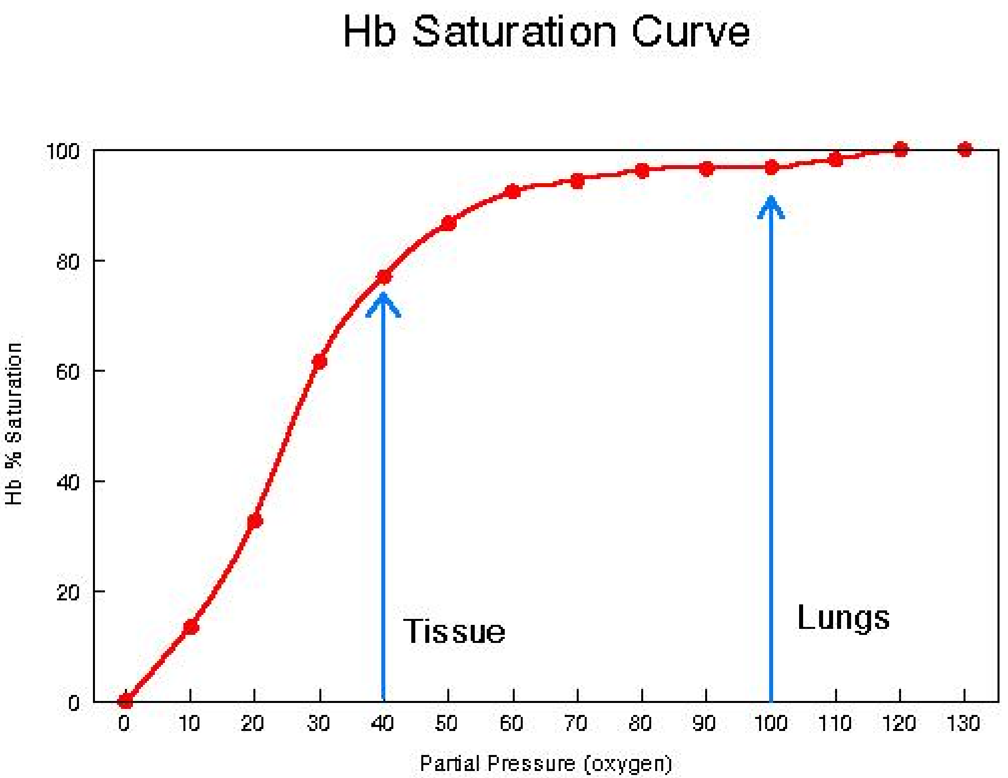
Hb(O2)3 + O2 <-> Hb(O2)4

Summary Reaction:

Hb + 4O2 -> Hb(O2)4



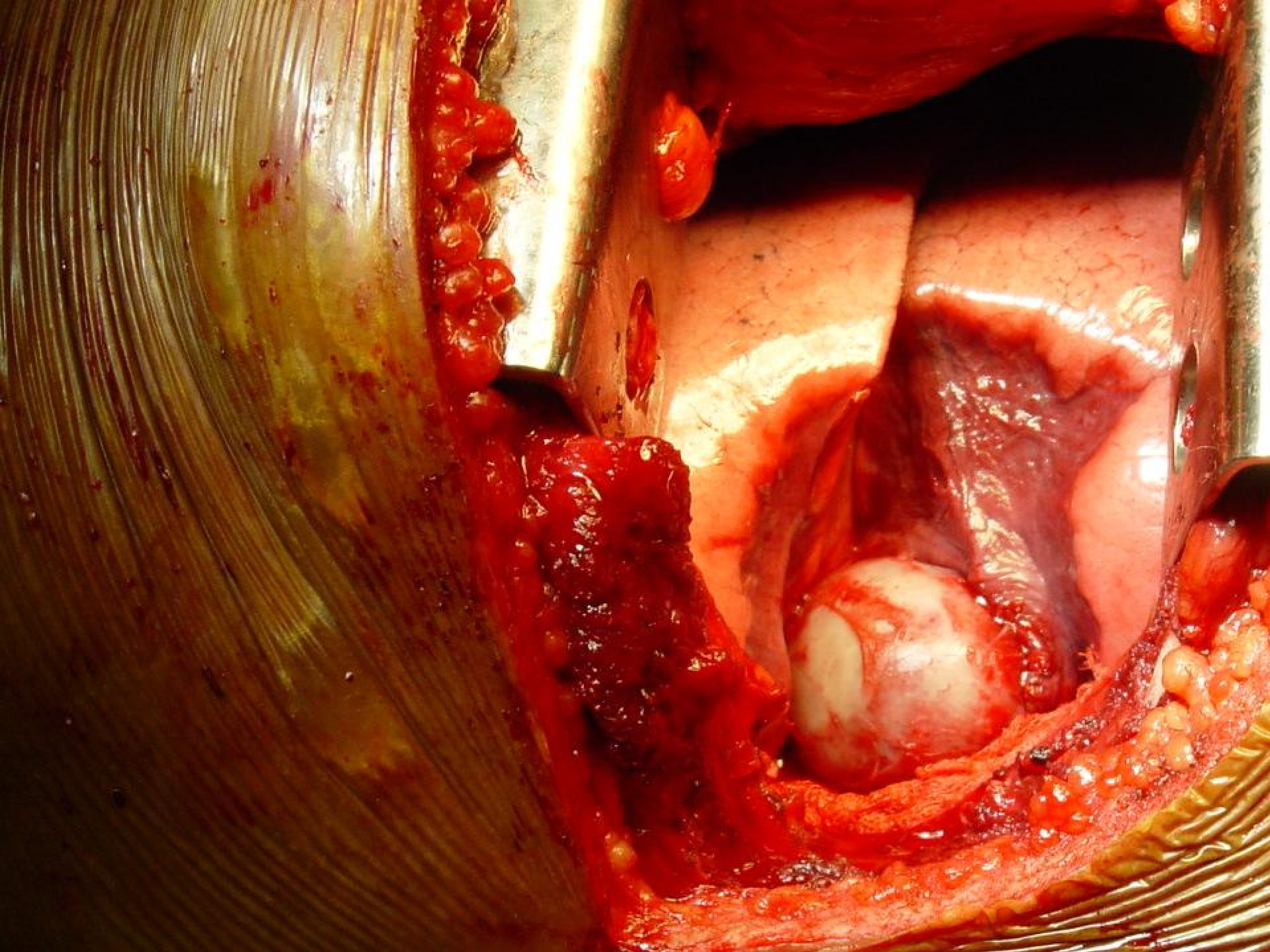
Heme

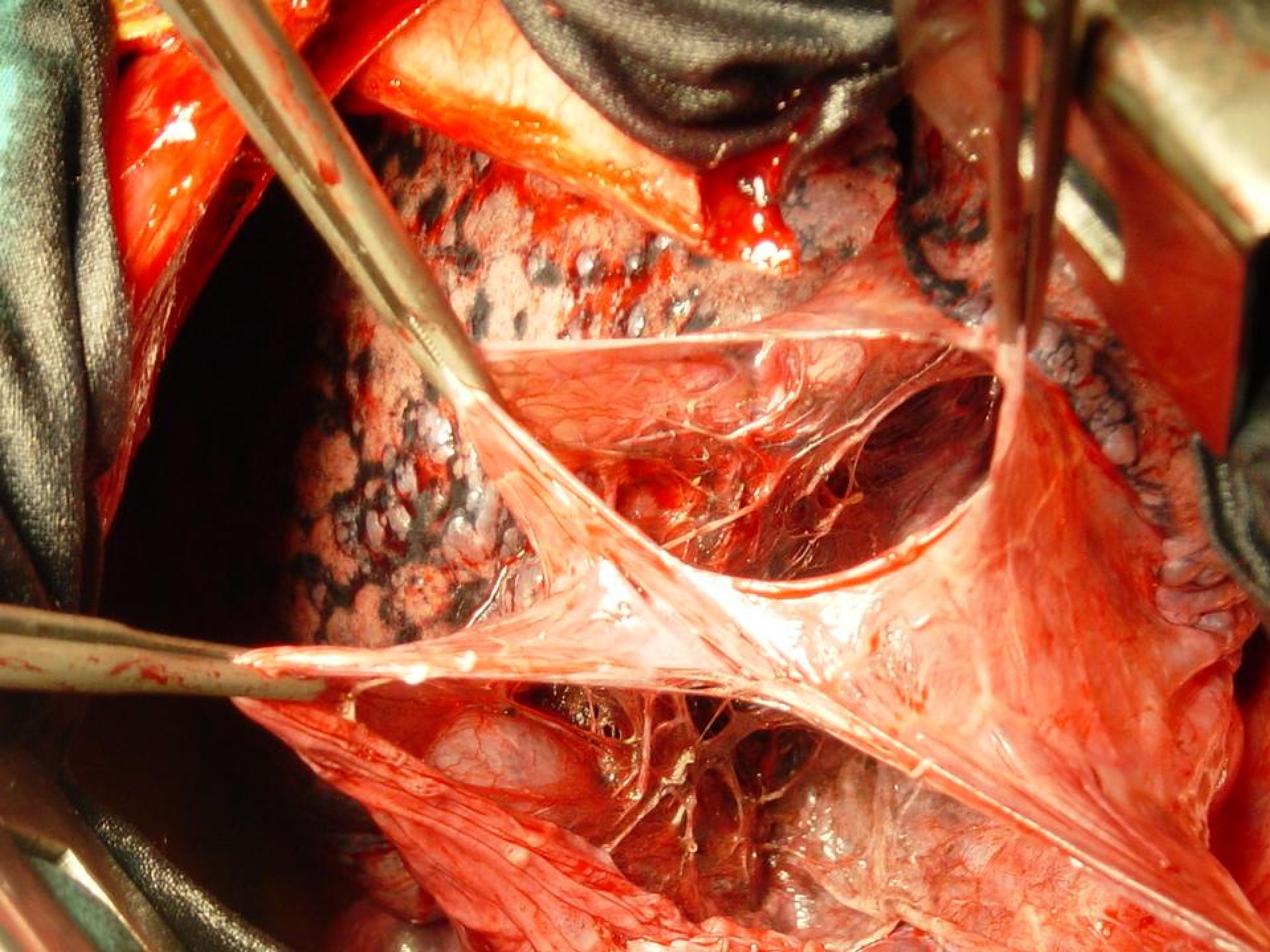


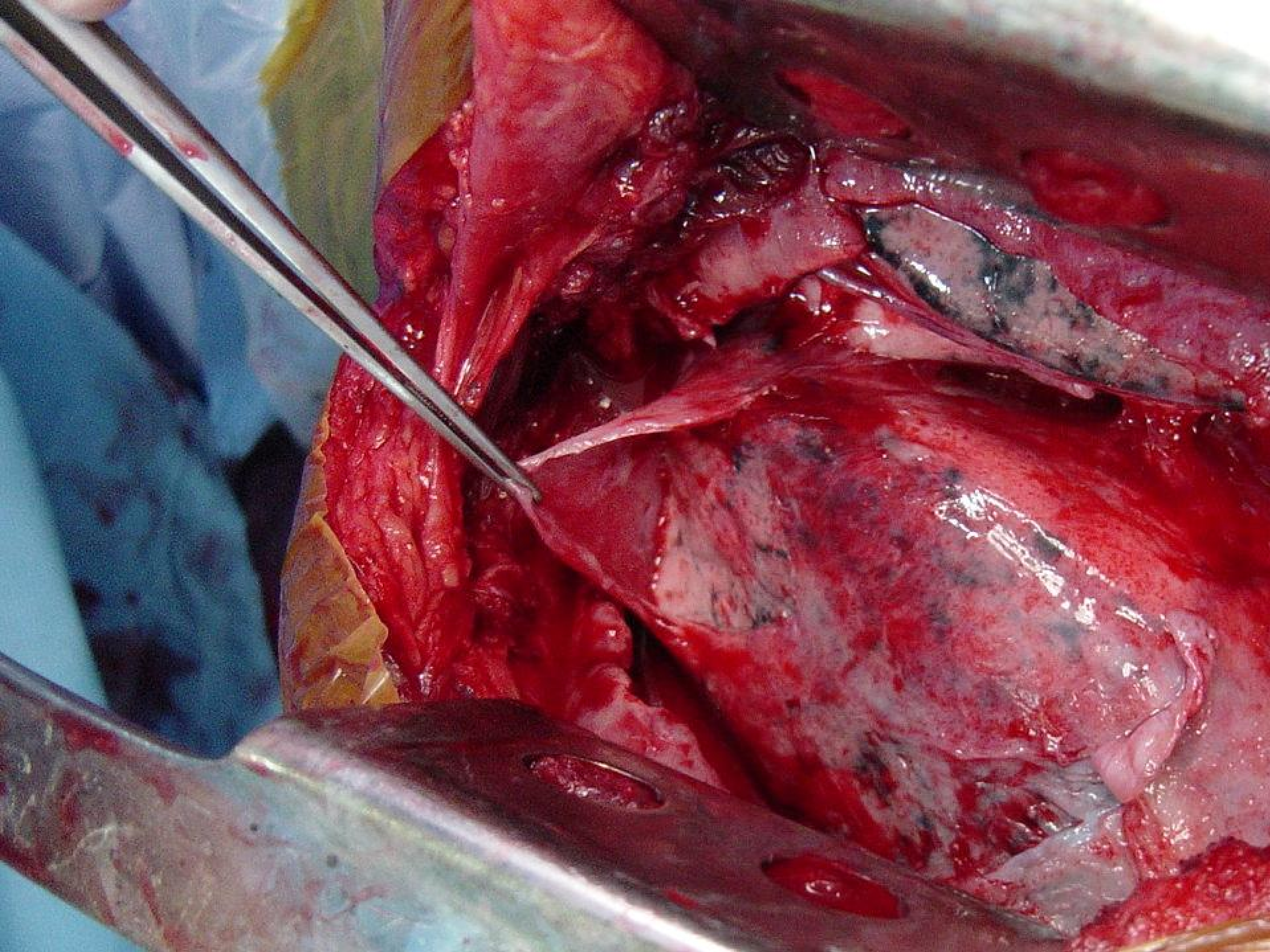
Hb Saturation Curve
100
80
60
40
20
0
Hb % Saturation
0 10 20 30 40 50 60 70 80 90 100 110 120 130
Partial Pressure (oxygen)
Tissue
Lungs

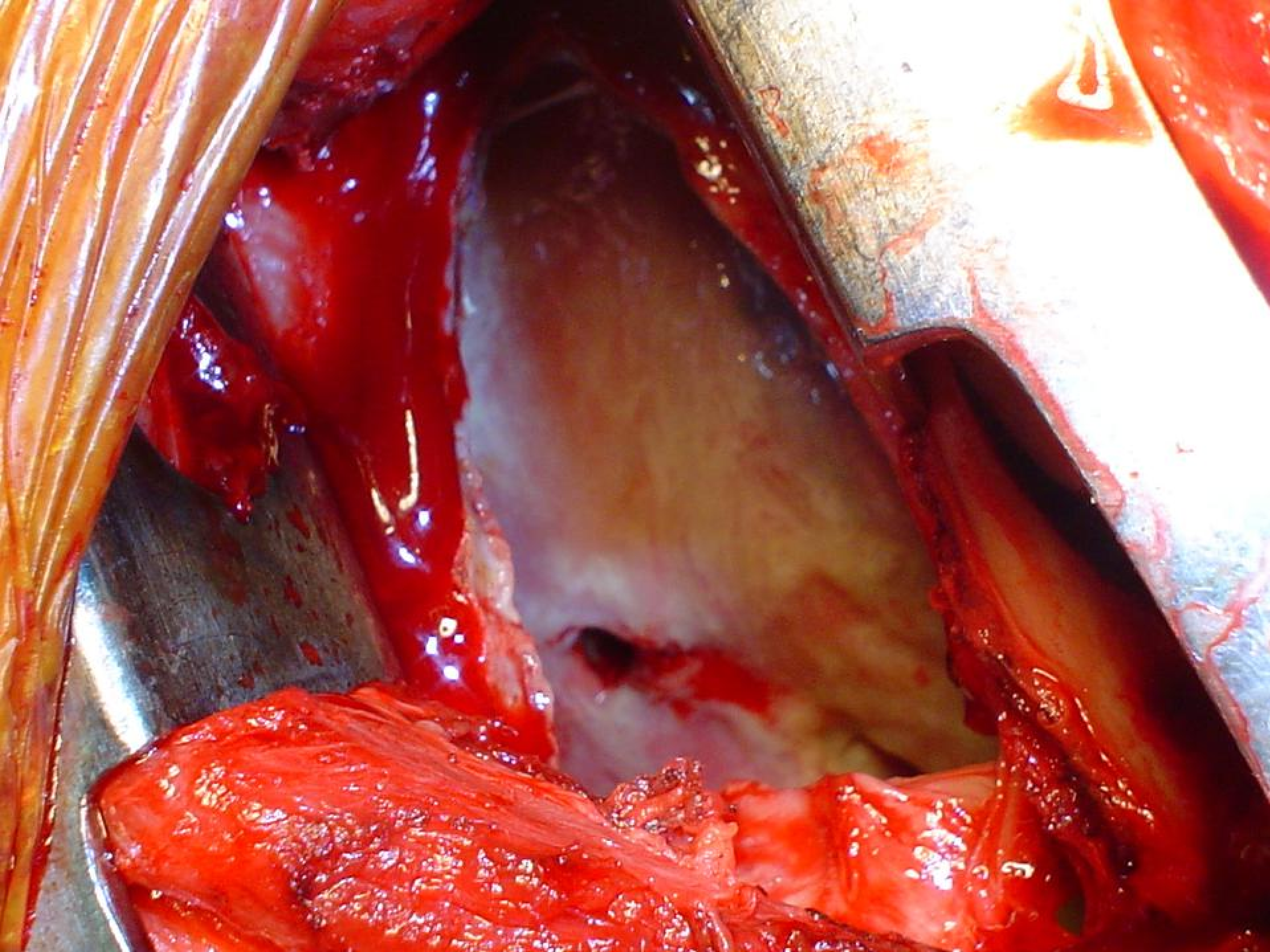
How do lungs get damaged?

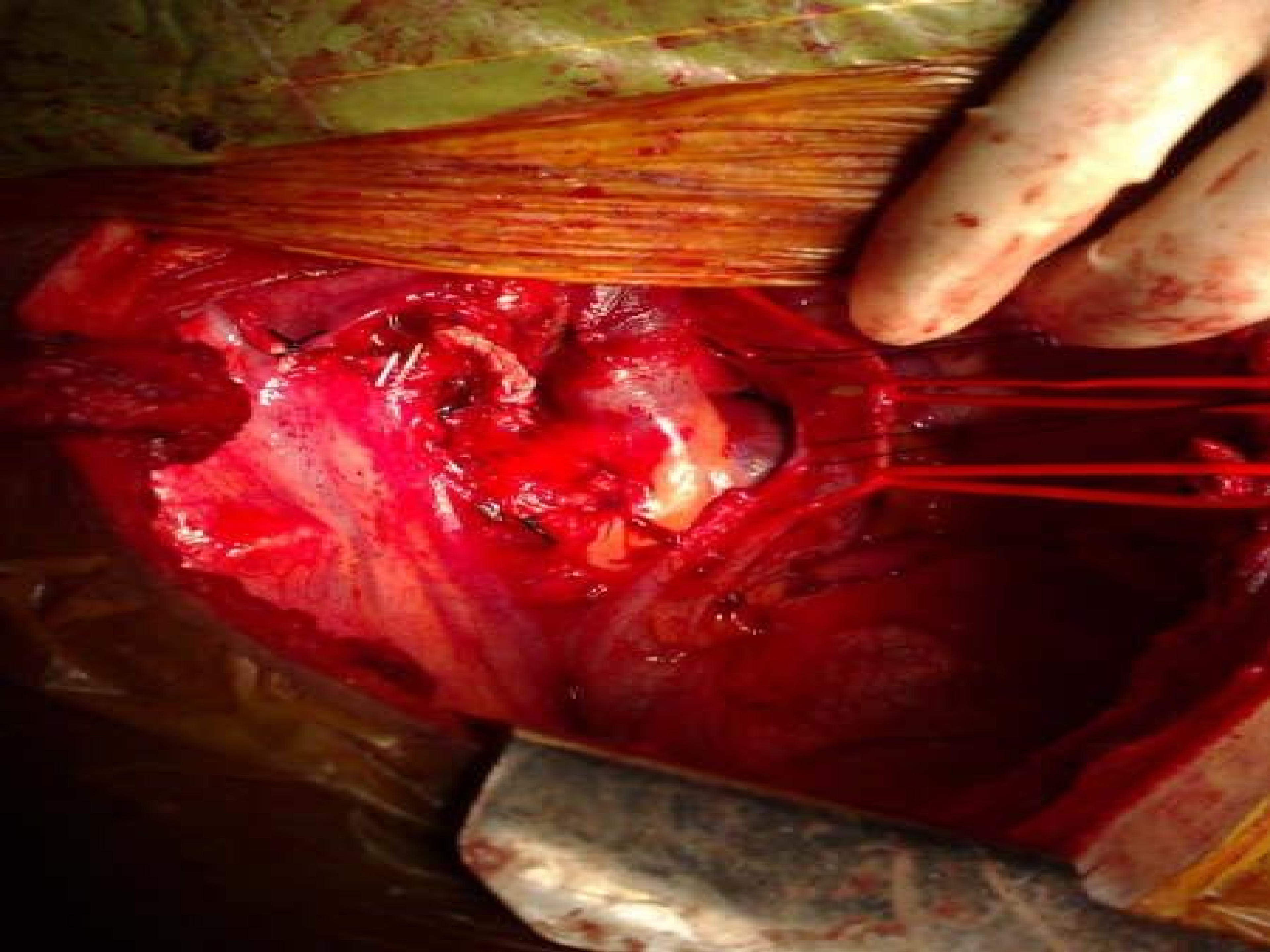
Normal CXR

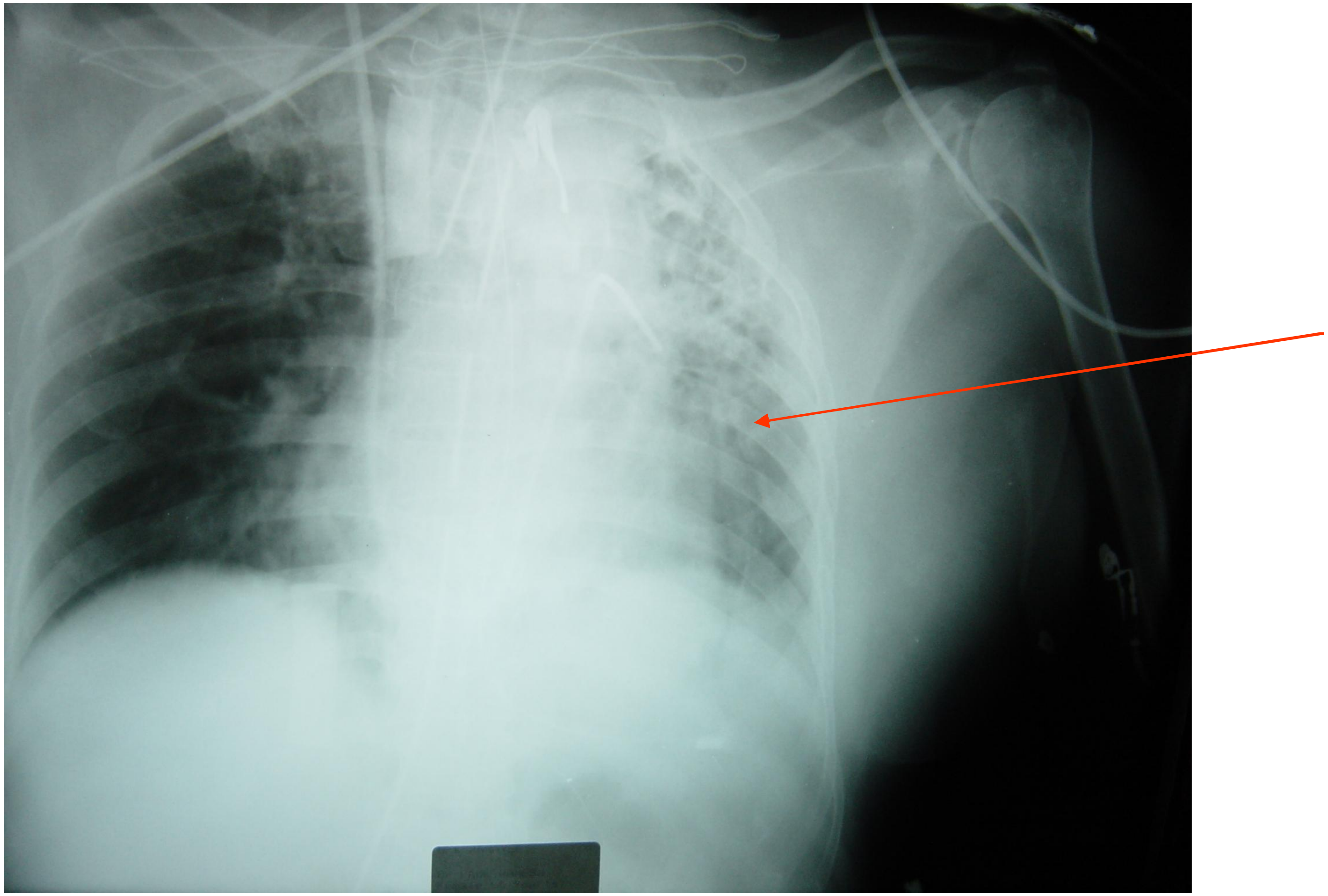












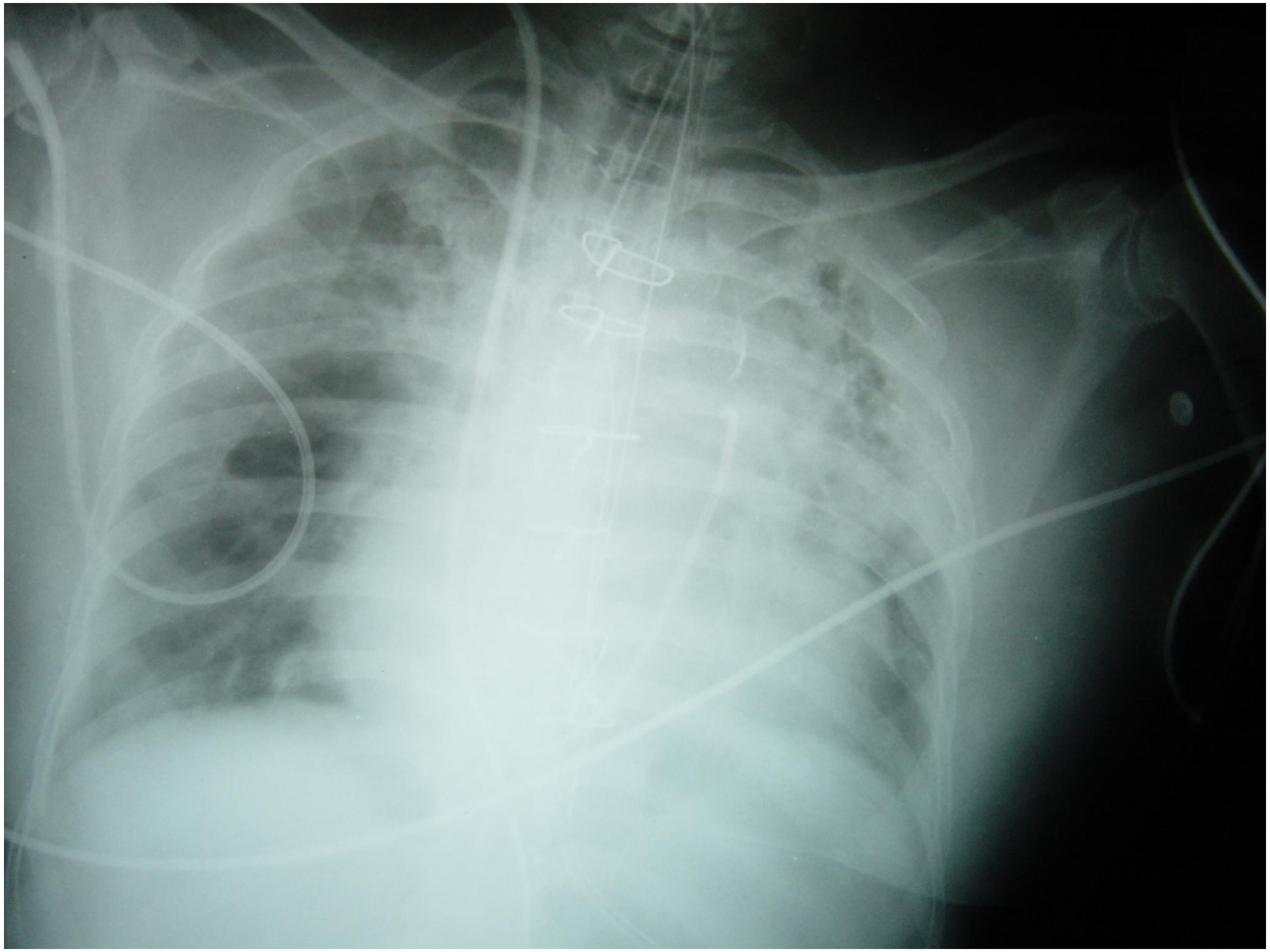


Table 2. Estimated annual health effects of indoor air pollution exposures in India

Disease	Deaths, thousands	YLL, millions	DALYs, millions	Sickday severity
I. Strong evidence				
ARI* (880,000)	270–400	9.2–14	9.6–14	0.28
COPD† (60,000)	20–35	0.19–0.34	0.39–0.68	0.43
Lung cancer† (6,000)	0.42–0.79	0.0045–0.0086	0.0048–0.0090	0.15
II. Moderate evidence				
Blindness† (~0)	~0	~0	0.064–0.13	0.5
TB† (250,000)	53–130	0.97–2.4	1.1–2.6	0.15
APO (560,000)	?	?	?	
Asthma (20,000)	3.6–9.0	0.046–0.12	0.27–0.68	0.15
III. Suggestive evidence				
IHD† (1,100,000)	54–200	0.49–1.8	0.55–2.1	0.32
Possible total (2,300,000)	400–780	11–18	12–20	
Range used§	400–550	11–16	12–17	

Estimates listed in order of the strength of evidence under Indian conditions. Mortality and conversion to life years lost and morbidity as in ref. 37. APO, adverse pregnancy outcomes. Severity is taken as the disability weighting in ref. 37 and varies from 0 (healthy) to 0.85 (severe disability). Indian total deaths for each disease are listed in parentheses.

*Under 5 years only.

†Women only.

‡Disability-adjusted life year = (years lost to premature death) + (years lost to disability) × (severity factor) (37).

§Full range for Class I plus low end of ranges for Classes II and III.

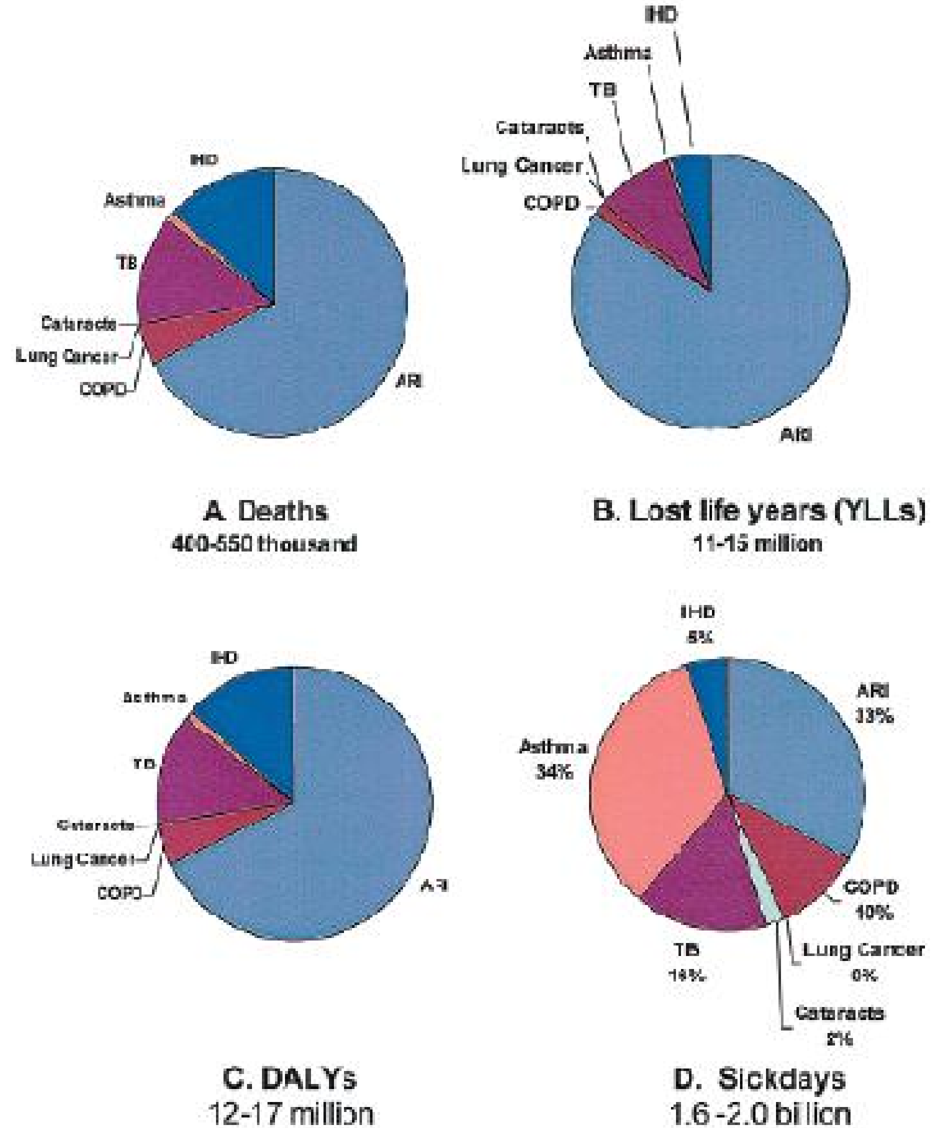


Fig. 1. Estimated distribution of the annual health burden from indoor air pollution in India in terms of deaths (*A*), YLL (*B*), DALYs (*C*), and sickdays (*D*).

Table 1. Estimate of annual premature mortality from air pollution in India (thousands of deaths)

Outdoor exp. ('000)	Indoor exp. ('000)	Pollutant used as indicator	Comments (ref.)
50–300	850–3300	PM	Using urban air quality data and rural exposures from rural microenvironment studies and urban distribution; MDC exposure-response information; range from spread between daily and annual studies (7)
40	—	PM	36 cities based on MDC exposure-response data (8)
86	—	PM/SO_x	Chinese exposure-response data (9)
84	590	PM	Using local air pollution monitoring data and Chinese exposure-response data (10, 11)
200	2,000	PM	Based on estimates of time and exposures in major microenvironments by important population groups and MDC exposure-response data (12)
52	—	PM	Extrapolation of ref. 8 with 1995 data (13)

Most of these estimates applied the pollutant-based method discussed in the text. exp, exposure.

Worldwide lung disease burden

- acute lung injury (ALI)/
-adult respiratory distress syndrome (ARDS)

- 30-50 per 100,000 has ARDS with a mortality of 40-60%

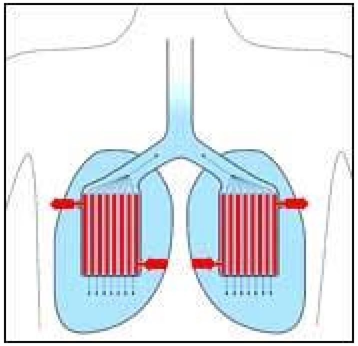
-Chronic obstructive pulmonary disease (COPD) has a prevalence of 11.6 in Men and 8.77 in Women per 1000 (WHO report)

-Lung Failure is the fourth leading cause of death worldwide.

Statistics on Pulmonary Disorders (USA)

- 350,000 American die of Lung disease
- 150,000 are affected by Adult Respiratory Distress Syndrome (ARDS)

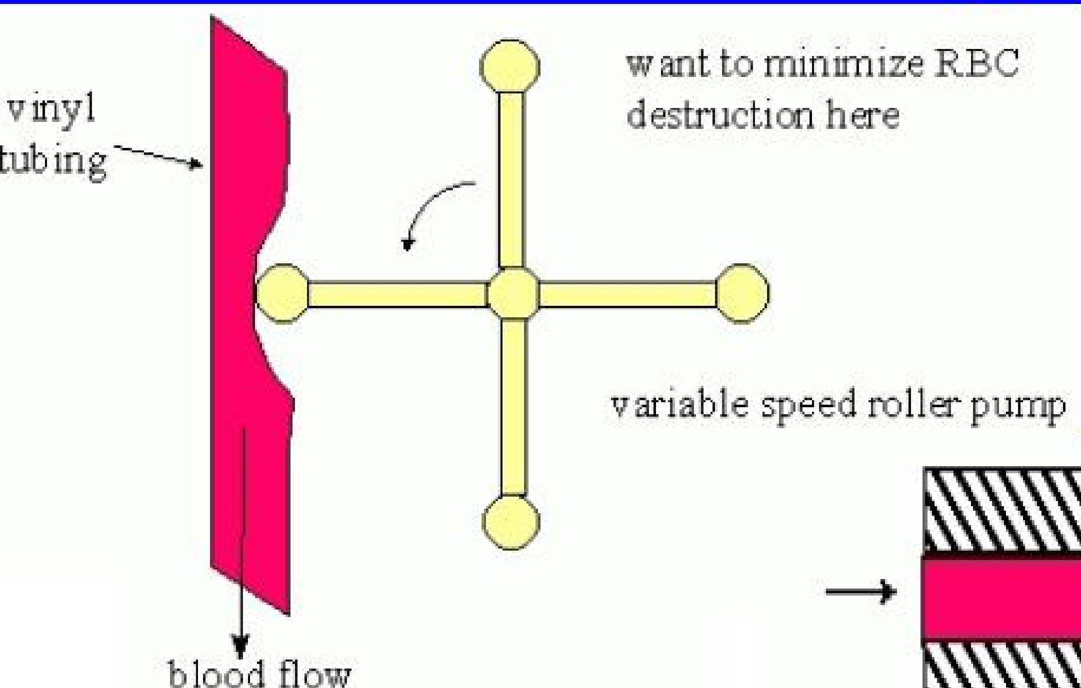
- 40-50% of ARDS mortality
- 400,000 patients are hospitalized for Chronic Obstructive Pulmonary Disease (COPD)

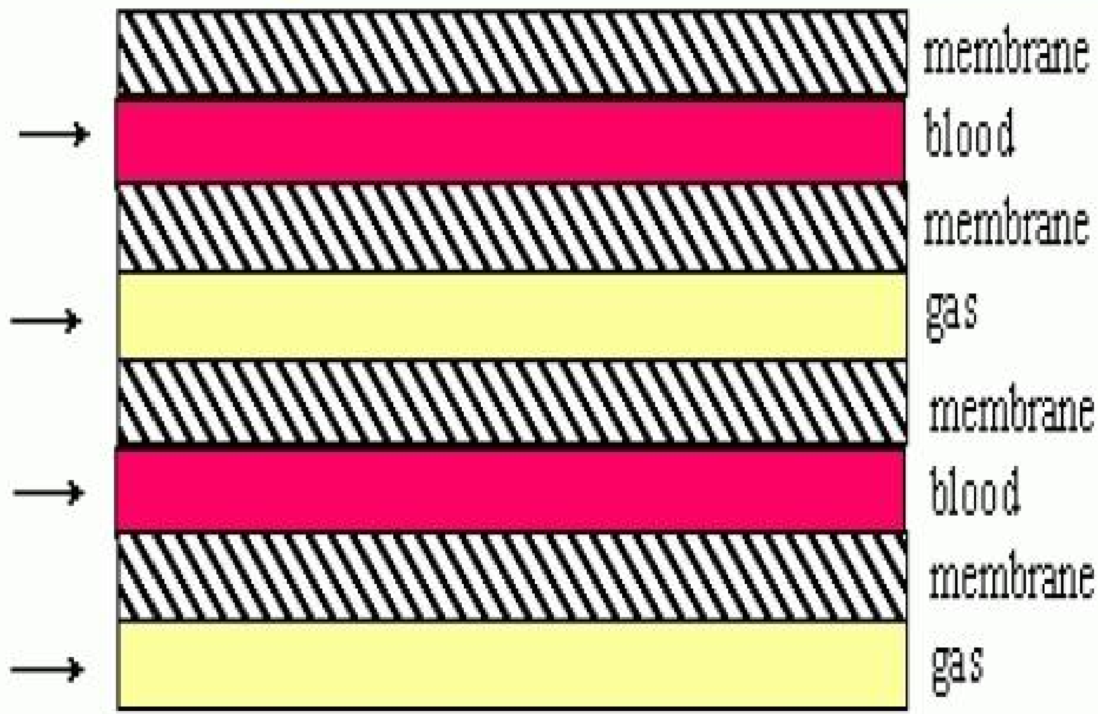


How to treat low oxygen levels?

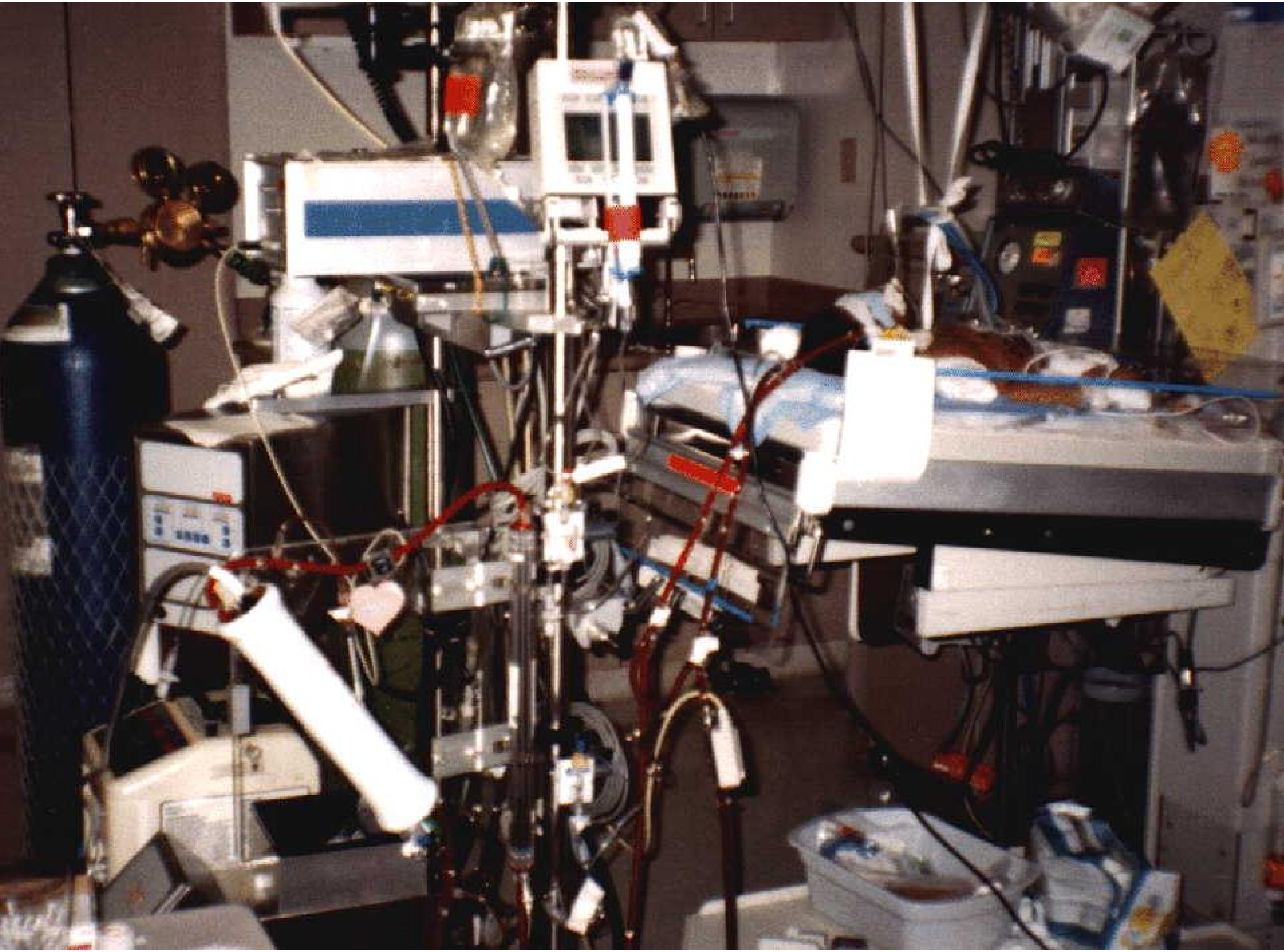

119
ICMM20
ICU
ICVN10
122
60
46
52
68

Heart Lung Machine






29 1828



Present day technology:

membrane Oxygenators

A little history (1954)

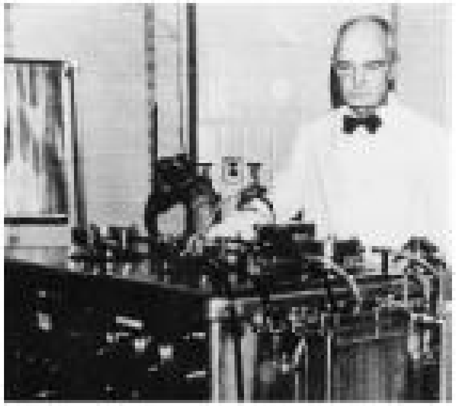
Why oxygenation?

- For lung failures and Pulmonary disorders
- By-pass surgeries

How it is done presently:

- **Heart lung machine: Gibbon, 1953**

  Closure of an atrial septal defect in an 18-year-old girl



Extra Corporeal Membrane Oxygenator (ECMO)

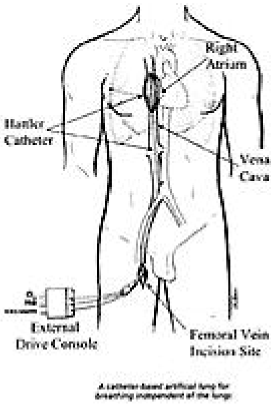
Heart Lung Machine

Oxygenerators Presently available:

1. Fiber Membrane Oxygenrators
2. Oxygenators in cardiopulmonary Bypass (CPB)
3. Extracorporeal membrane Oxygenraors (ECMO)

Natural Lungs:

- Alveolar –capillary area ~ Tennis court surface (100-150 m^2)
- gas exchange rate ~ 200-250 ml/min in average adults
- Area to volume ratio (A/V) ~ 290 cm-1
- VO2 ` 210- 3200 ml/min



The Road Map :

Current

External Blood Circuit
CPB and ECMO
Temporary Support

Next generation

Integrated Pump/ Oxygenator
Wearable
Temporary to semi permanent

Intracorporeal

Intrathoracic

Surgical implant
Semi-permanent

Intravenous
Percutaneous Insertion
Temporary support

Best and total solution is: Lung Transplant

Introducing a revolutionary concept in blood oxygenation

What is photocatalytic reaction?

The concept:

- Photo catalysts are used for splitting water into oxygen and hydrogen

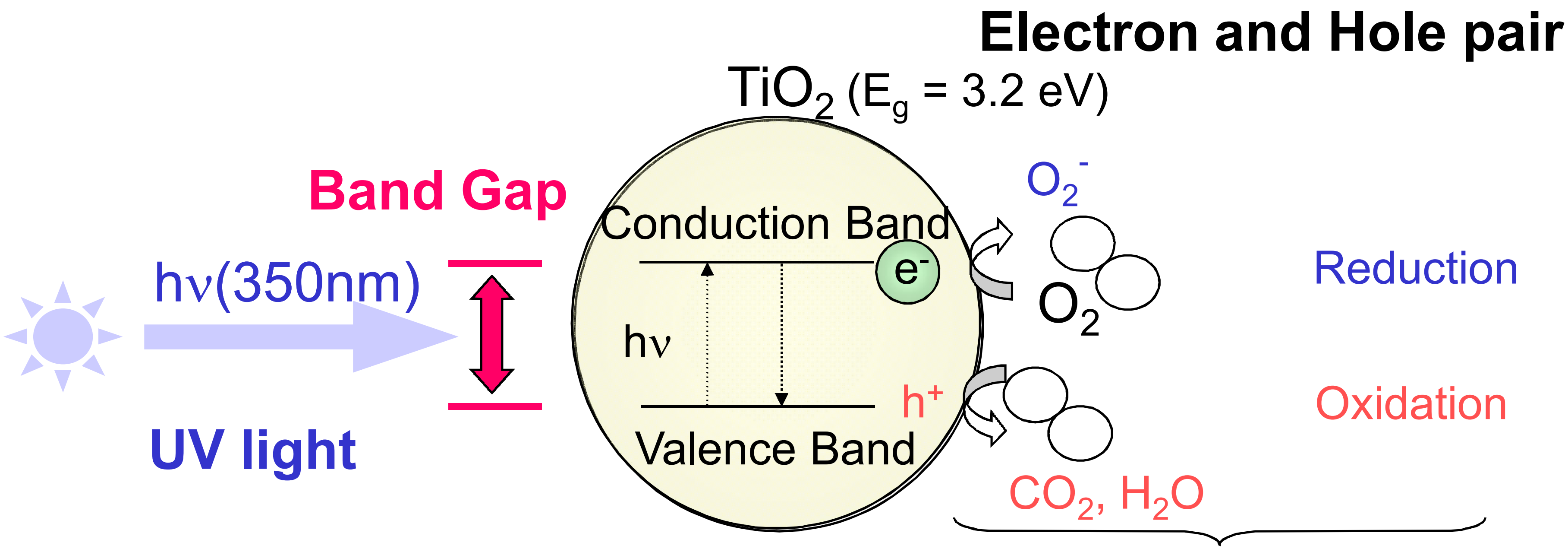
- TiO_2 is a well known catalyst
- these catalysts are used extensively and the photo physics and chemistry is well known

- Basically these catalysts are Semiconductor materials

Why not use these catalysts to split water available in the blood to generate oxygen ?

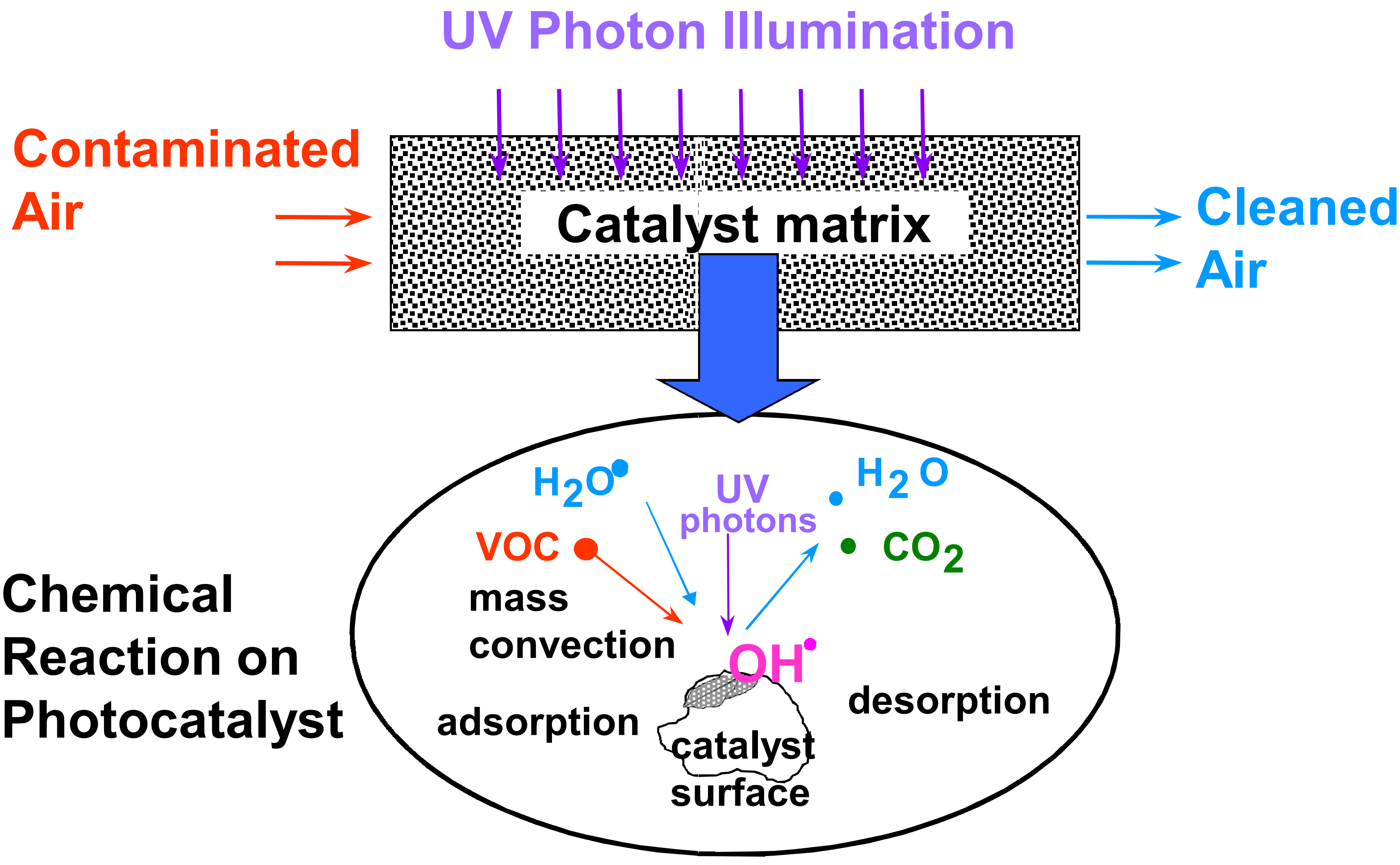
Photocatalysis – Physical Chemistry

Features low-temperature (30-80 C) oxidation technology



13.9-16.0 kJ mol^{-1} activation energy
(Fu et. al. *J. Photochem. Photobiol. A: Chem.*, 1996)

Photocatalytic Processing of Air



What we are envisaging of Photocatalytics:

- Oxygenation of human blood

- generate oxygen at high altitudes

- generate oxygen in deep mines

Why not develop this technology for space travel?

What we did:

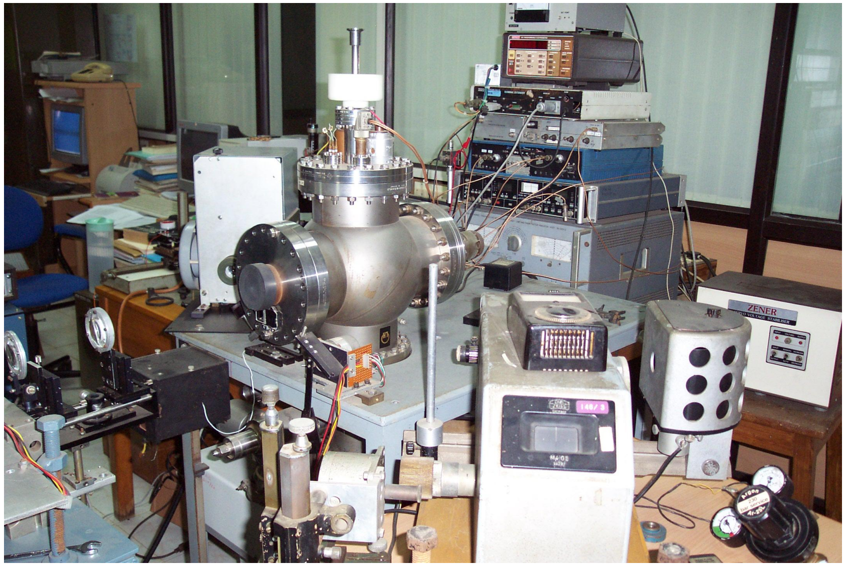
- Designed a photolytic cell
- Prepared Thin Films of Titanium dioxide and indium tin oxide

(This films are a big part of our daily life)

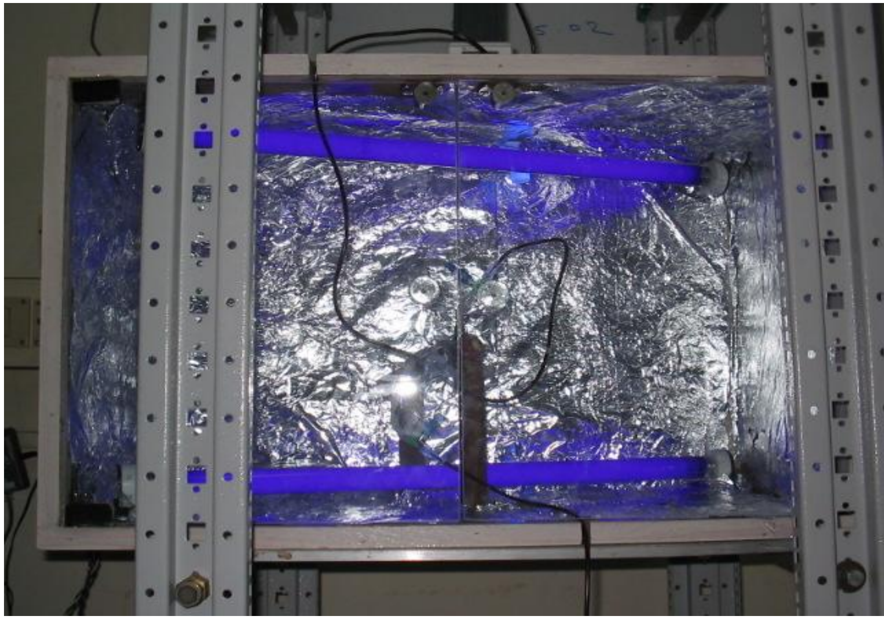
- Conducted the photocatalytic experiment on deoxygenated blood

(Deoxygenated blood looks blackish)

Fully oxygenated blood looks Blood Red !!



Kelvin Probe

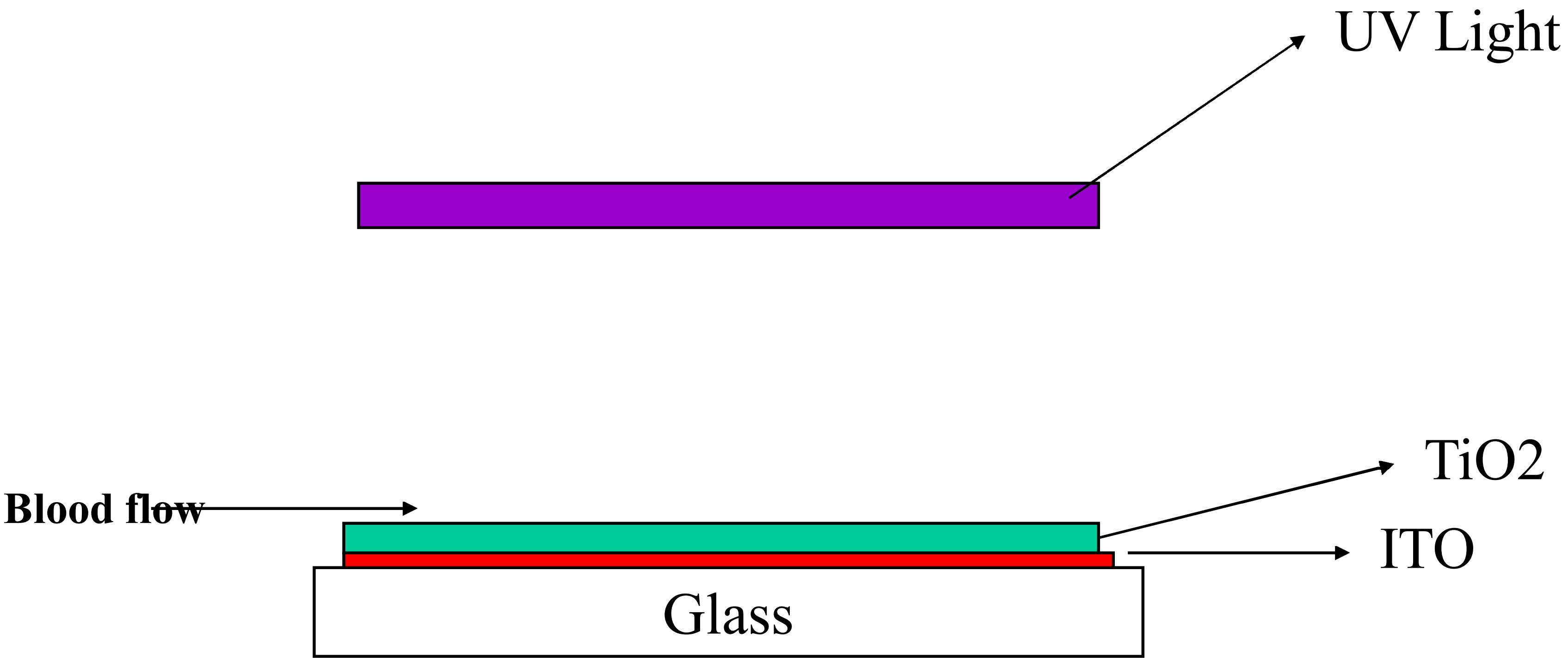


The UV Chamber

DC Magnetron Sputtering System

The initial work carried out in our laboratory and the results

We did the work and filed a Patent : 427 Che 2006 dated 10 March 2006



We did the experiment on Human blood

ITO and TiO_2 have been deposited by DC magnetron Sputtering

TiO_2 is in nano form ~ 30 -40 nm

We measured the oxygen infused into blood by

1. Optical methods
2. By Blood Gas Analyzer (machine used by Surgeons)

Experimental method

- Venous blood (20mls) drawn after maximal exercise
- 10mls in photocatalytic cell (Test)
- 10mls in control cell of same construction and dimensions as Test without Tio2/ITO thin film coating (Control)

Measured variables

- Baseline, 2hr control and 2hr test blood gas analysis done (po_2, Sao_2)
- pH
- Hematocrit
- Serum osmolality
- Serum potassium
- Peripheral smear

Measurement of whole blood oxygen content (CaO_2)

- [(1.34 x Hb g/dL x SaO_2 (expressed as fraction)] + (.003 x PO_2 mm of Hg)

Absolute increase in whole blood oxygen content (CaO2) post photocatalytic reaction

	Baseline CaO2	2hr Control CaO2	2hr Test CaO2	Absolute increase in CaO2
Sample 1	8.19	9.1	19.18	10.08
Sample 2	11.87	12.65	20.82	8.17
Sample 3	3.35	4.17	20.12	15.95
Sample 4	7.39	11.3	20.56	9.29
Sample 5	6.5	8.53	15.43	6.9

Results

	Baseline (mean)	Control (mean)	Test (mean)
Serum potassium	4.2	4.4	4.5
Serum osmolality	247	279	314
Hematocrit	43	43	44
pH	7.18	7.19	7.18

Peripheral smear

	Baseline	Control	Test
RBC hemolysis	None	None	None
Platelet aggregation	None	None	None

Limitations

- In vitro
- Static blood column

Conclusion

- Consistent oxygenation of blood
- Quantum of oxygenation variable
- No significant RBC lysis, platelet aggregation
- No significant drop in pH
- Further dynamic experiments underway

Absolute increase in percent saturation of hemoglobin (SaO2) post photocatalytic reaction

	Baseline SaO2	2hr Control SaO2	2hr Test SaO2	Absolute increase in SaO2
Sample 1	37.9	42	88.7	46.7
Sample 2	54.9	58.5	96	37.5
Sample 3	15.4	19.2	93.1	73.9
Sample 4	34.1	48.2	94.6	46.4
Sample 5	32	42	76	34

Absolute increase in dissolved oxygen content (pO2) post photocatalytic reaction

	Baselinepo2	2hr Controlpo2	2hr Test pO2	Absolute increase in pO2
Sample 1	23	27	54.7	27.7
Sample 2	33.7	37.1	80.8	43.7
Sample 3	17	17.9	78.8	60.9
Sample 4	25.6	32.4	92.1	59.7
Sample 5	23	29	50	21

Average increase in oxygen post photocatalytic reaction

- Mean increase SaO2 – 47.7%
- Mean increase Po2 – 42.6 mm Hg
- Mean increase in CaO2 – 10.1ml of oxygen /100mls of blood

Till now:

- We have shown the Proof of concept of effective oxygenation in human blood using Photocatalytic action
- We have further demonstrated consistent oxygenation
- The materials employed are Bio-compatible
- We have shown *in vitro* that there is no damage to the Blood cells and Platelets

We are presently working on :

- To bring the Photocatalytic action from UV to Visible

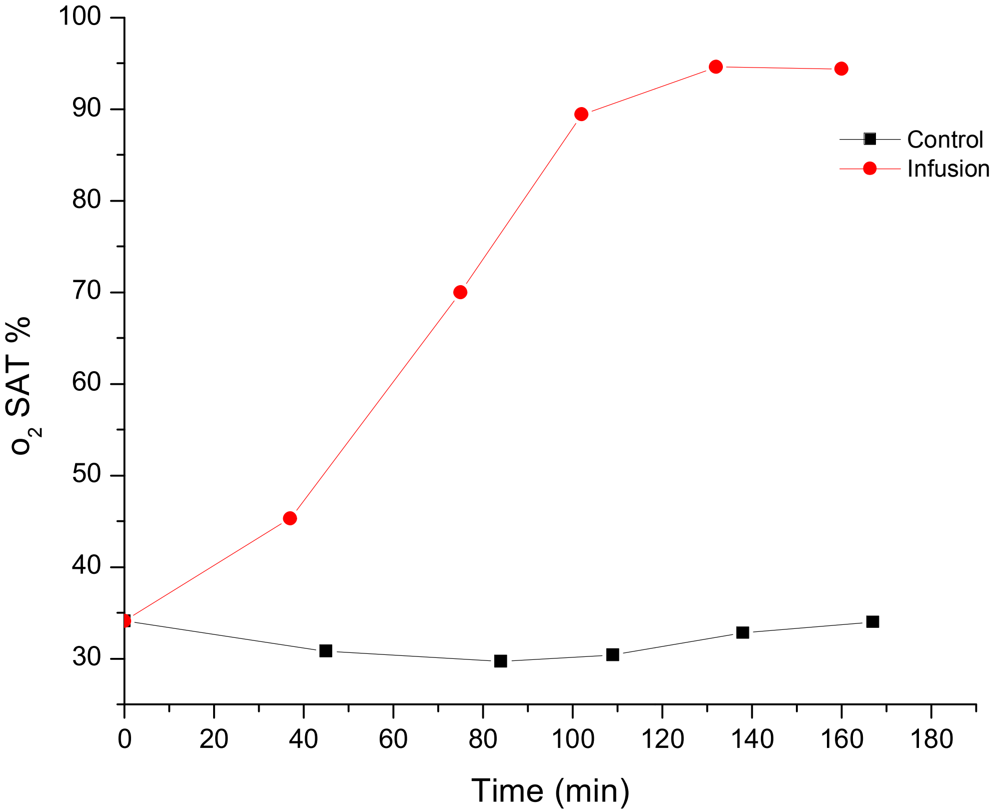
- DNA analyses is currently being done

- Dynamic experiments are underway

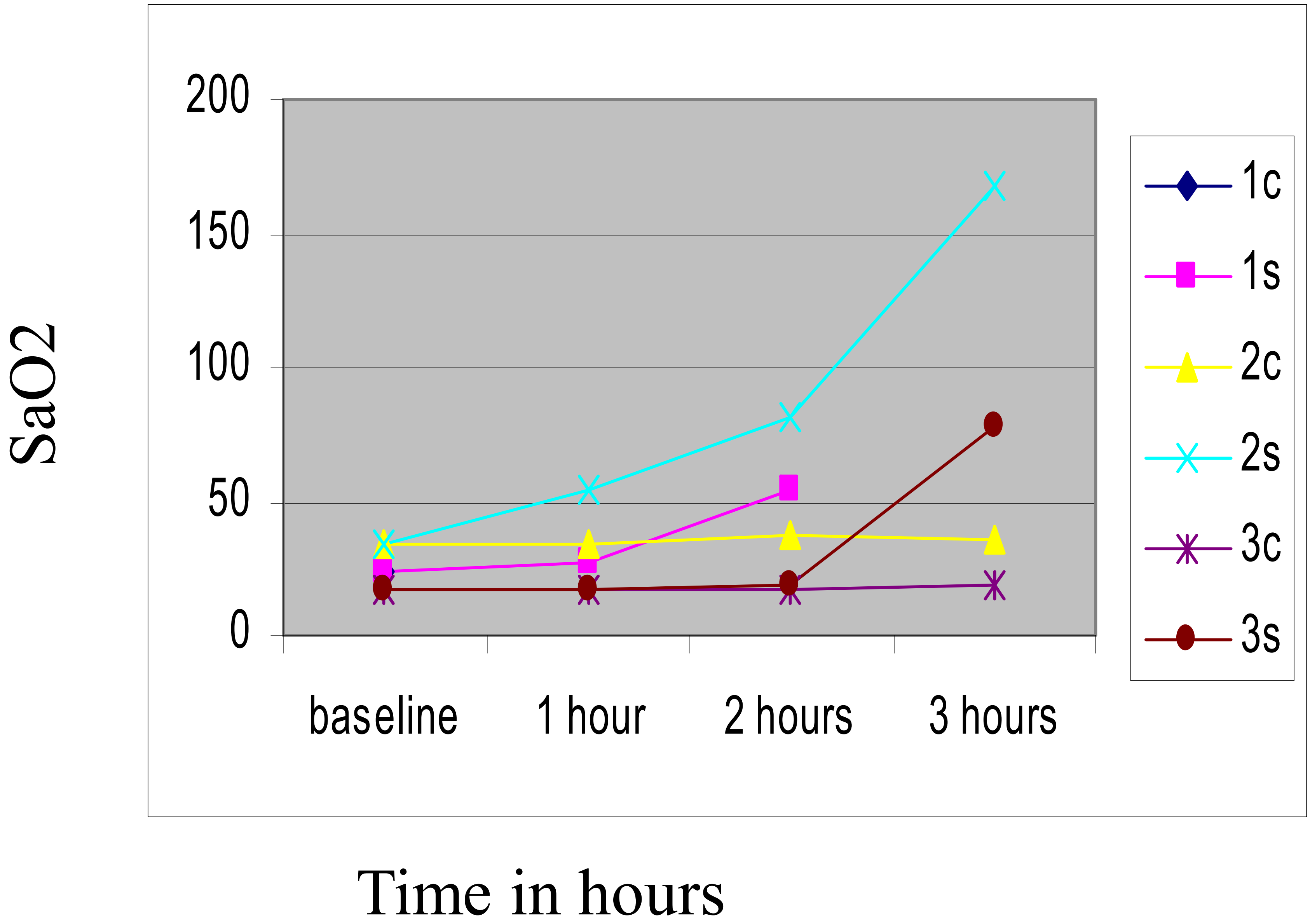
- Qunatification and accurate control ofoxygen generation

- Initiate Animal trials for demonstrating safety in an *in vivo* model

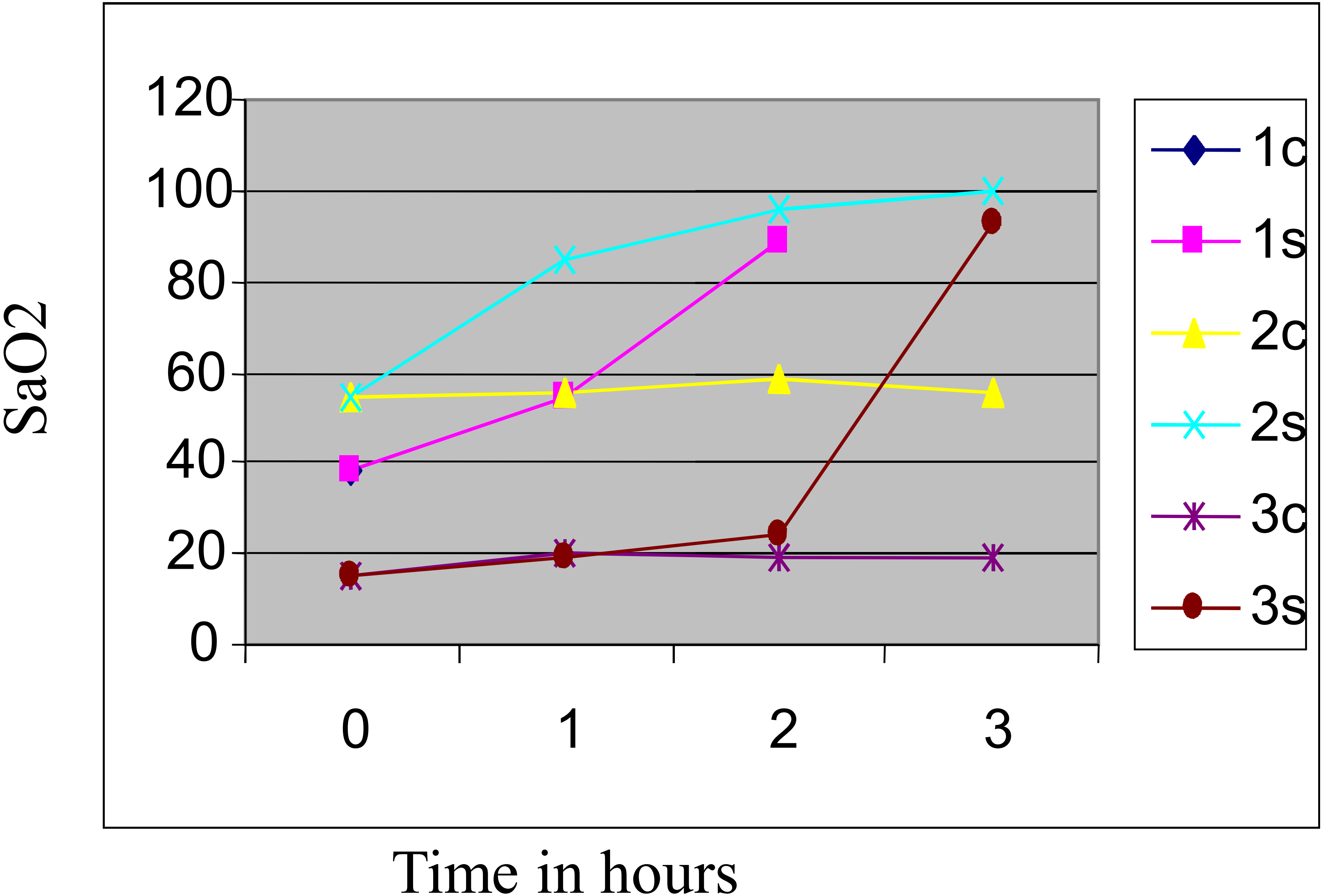
We are also addressing the question of removal of CO_2 from the System



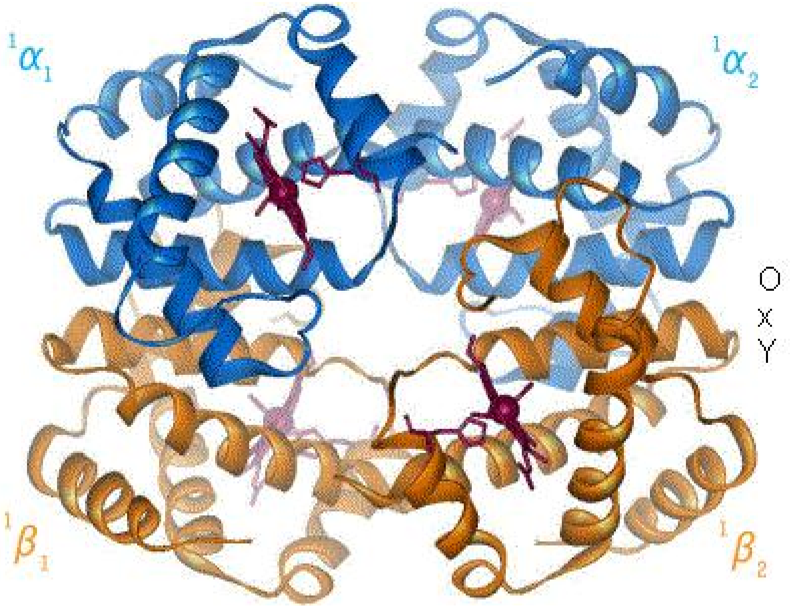
100
90
80
70
60
50
40
30
o_2 SAT %
0
20
40
60
80
100
120
140
160
180
Time (min)
Control
Infusion

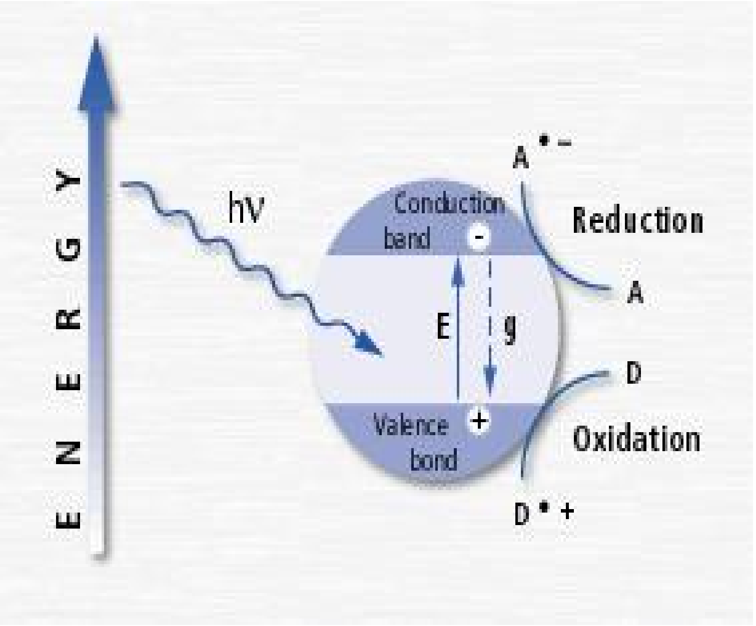


SaO2
200
150
100
50
0
baseline
1 hour
2 hours
3 hours
1c
1s
2c
2s
3c
3s
Time in hours



SaO2
120
100
80
60
40
20
0
0
1
2
3
Time in hours
1c
1s
2c
2s
3c
3s





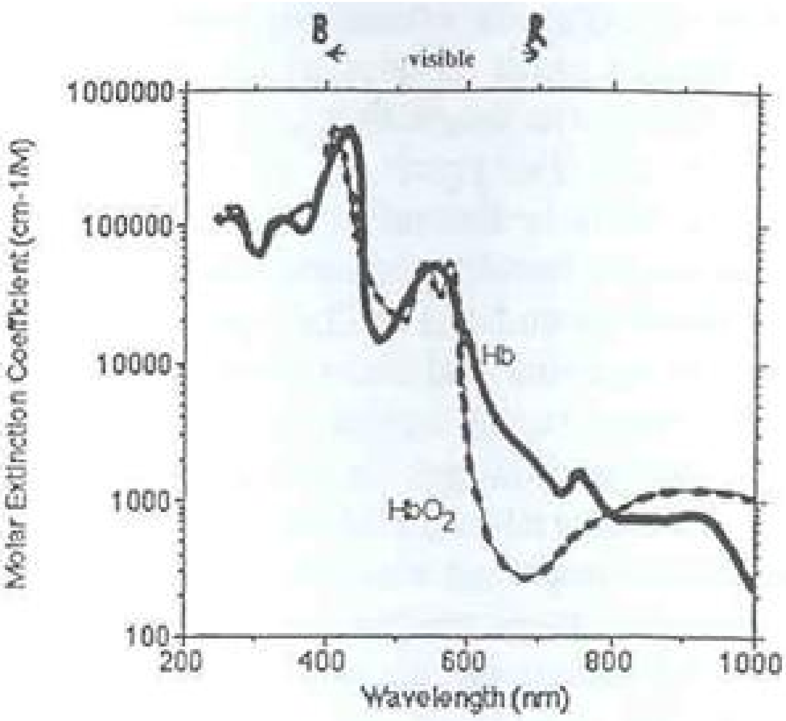
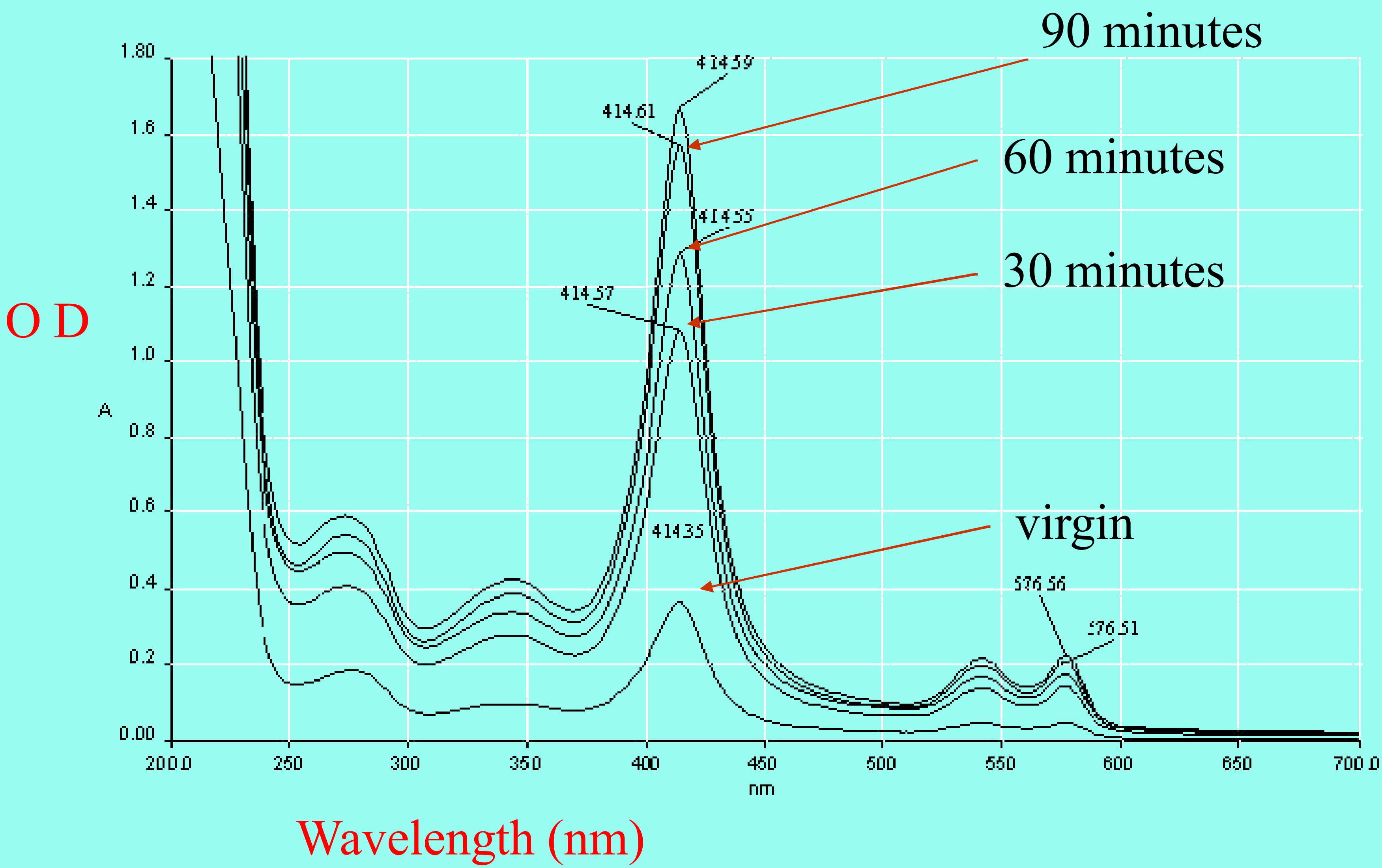


Figure 11 UV-visible Spectra of oxy- (HbO_2) and deoxyhaemoglobin (Hb)

Sample 3

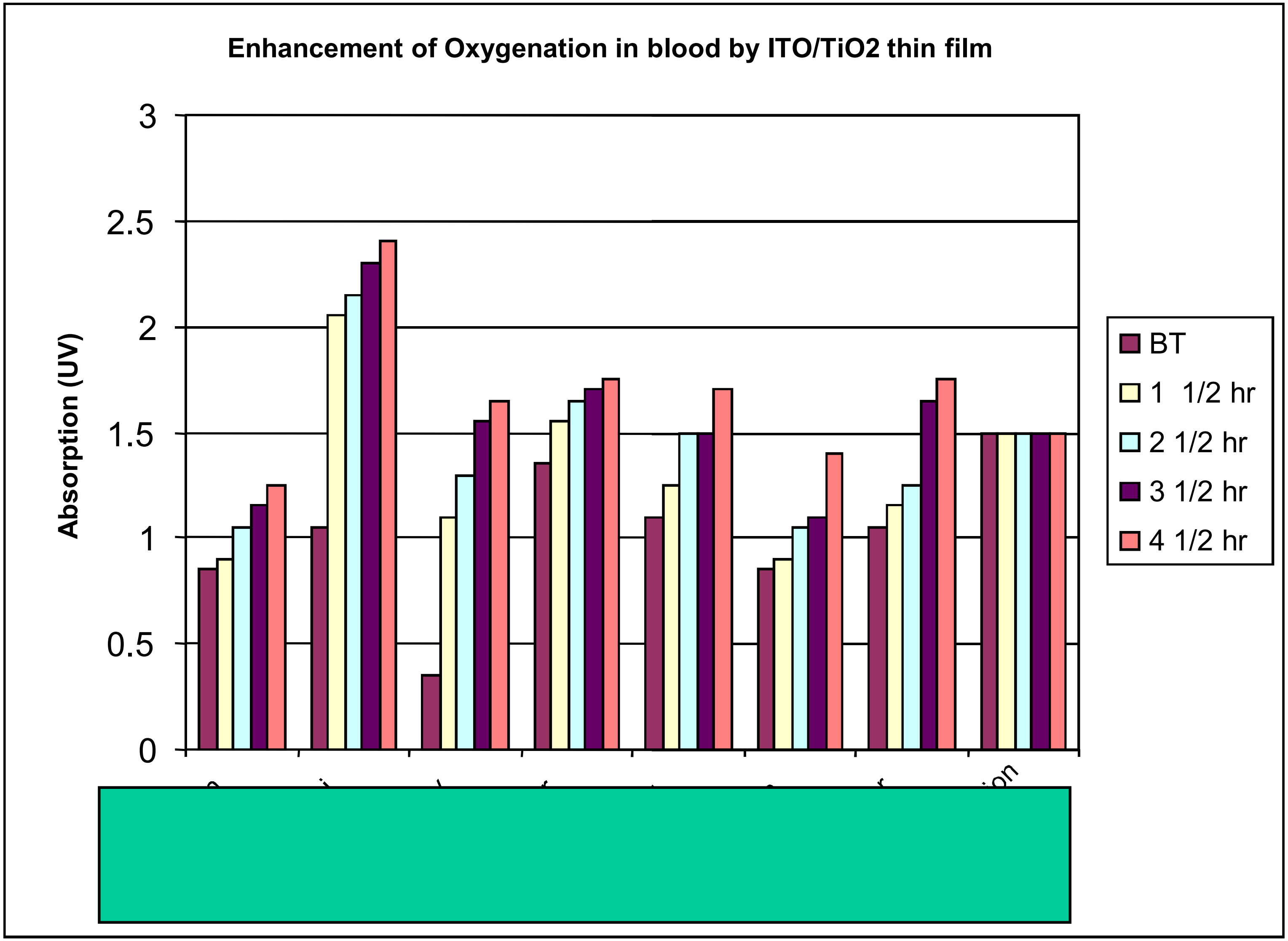
Optical Density of Hemoglobin

(These results are Patented)



Case study

B/G	B-treat	S1-1/2	S2-1/2	S3-1/2	S4-1/2	O2%	PULSE	HB%	RBC	PVC%	Age	Weight Kg
B+	0.85	0.9	1.05	1.15	1.25	98	74	18.1	5.67	49.4	27	55
A1B+	1.05	2.05	2.15	2.3	2.4	99	68	14.6	4.71	42	24	70.5
O+	0.35	1.1	1.3	1.55	1.65	98	68	15.1	4.86	42	27	59
A1+	1.35	1.55	1.65	1.7	1.75	99	87	14.4	4.61	41.4	38	80
O-	1.1	1.25	1.5	1.5	1.7	97	74	15.5	4.85	42.7	52	77
O+	0.85	0.9	1.05	1.1	1.4	98	63	15.2	4.55	40.5	26	67.5
B+	1.05	1.15	1.25	1.65	1.75	97	82	16.3	4.57	43.4	24	48.5
B+	1.5	1.5	1.5	1.5	1.5							


Enhancement of Oxygenation in blood by ITO/TiO2 thin film
Absorption (UV)
3
2.5
2
1.5
1
0.5
0
BT
1 1/2 hr
2 1/2 hr
3 1/2 hr
4 1/2 hr

What we plan to do :

The Problem has Two parts:

1. Material aspects
2. Oxygenation efficacies and blood related understanding

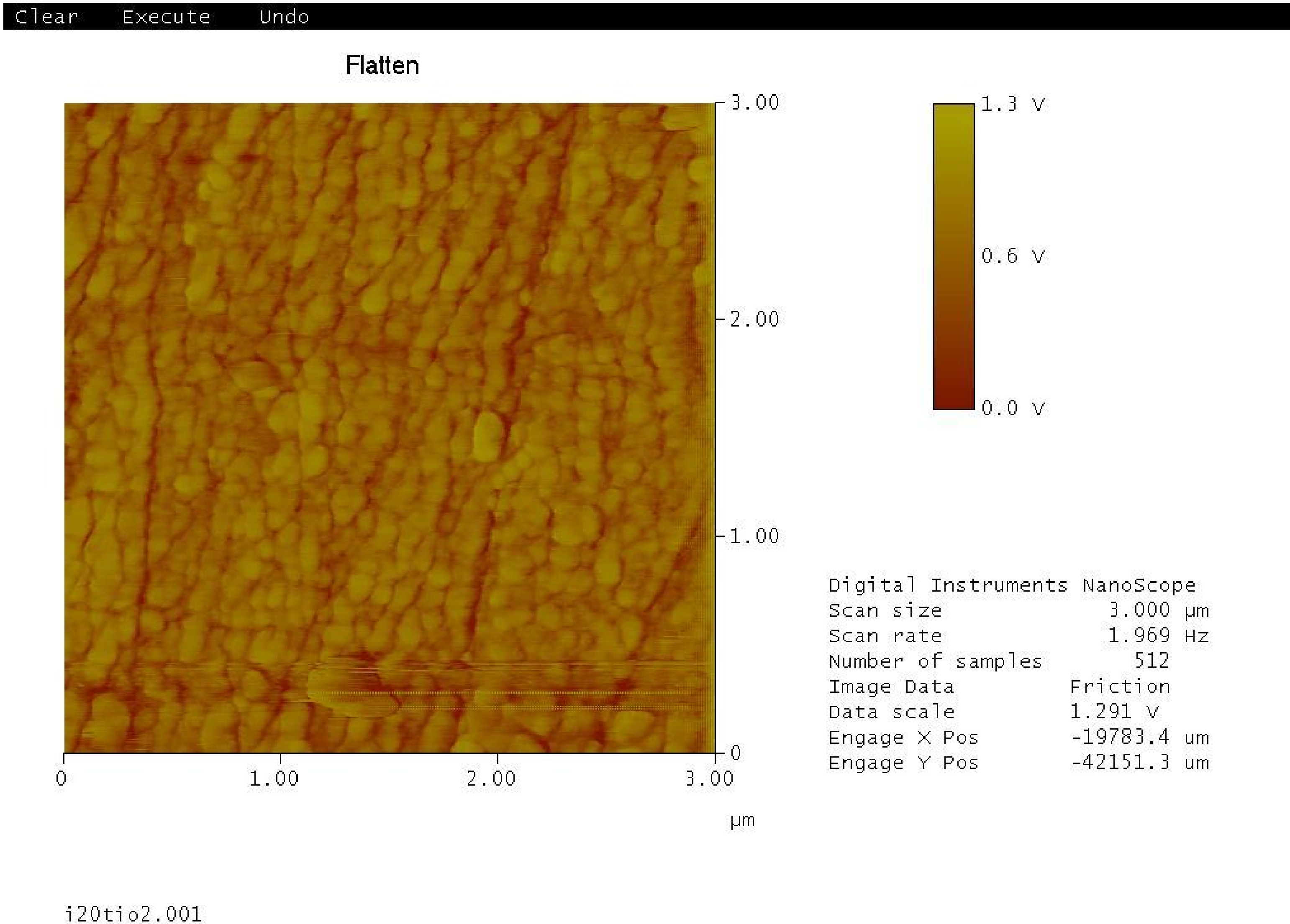
Material aspects

1. Photocatalytic efficiency
2. Visible wavelengths
3. Quantification of efficacy
4. Band gap engineering
5. New and novel Materials

Oxygenation

1. Biocompatibility
2. Hematocryt and Osmolality
3. Hemolysis
4. DNA and Reactive Oxygen
5. Animal experiments

ITO/TiO2 AFM:



Clear Execute Undo
Flatten
3.00
2.00
1.00
0
0
1.00
2.00
3.00
µm
1.3 V
0.6 V
0.0 V
Digital Instruments NanoScope
Scan size 3.000 µm
Scan rate 1.969 Hz
Number of samples 512
Image Data Friction
Data scale 1.291 V
Engage X Pos -19783.4 um
Engage Y Pos -42151.3 um
i20tio2.001

So far (past two years), we

- Have published TWO papers (ASAIO, AO)
- Third paper is under review
- Filed One Indian patent
- Presented One paper in 53 ASAIO Conference (Chicago) June 07-09, 2007.

Filed an Indian Patent :

This concept is tried in mammalian blood and cerum:

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Progress towards development of a photolytic artificial lung

P.M. Martin[a,*], B.F. Monzyk[b], E.C. Burckle[b], J.R. Busch[b], R.J. Gilbert[c], K.A. Dasse[d]

[a] *Pacific Northwest National Laboratory, 902 Battelle Blvd, MS K3-59, Richland, WA 99352, USA*
[b] *Battelle Memorial Institute, 505 King Ave, Columbus, OH 43210, USA*
[c] *Massachusetts Institute of Technology, 77 Massachusetts Ave., Cambridge, MA 02139, USA*
[d] *Levetronics, Levitronix Medical, 85 First Ave, Waltham, MA 02451, USA*

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Domen , et al. March 8, 2005

Inventors:	**Domen; Kazunari** (Kanagawa, JP); **Hara; Michikazu** (Kanagawa, JP); **Takata; Tsuyoshi** (Kanagawa, JP); **Hitoki; Go** (Kanagawa, JP)
Assignee:	**Japan Science and Technology Agency** (Kawaguchi, JP)

Photocatalysts for decomposition of water by visible light

Abstract

A photocatalyst which contains at least rhombic tantalum nitride or consists of rhombic tantalum nitride. A photocatalyst wherein said photocatalyst loads a promoter composed of transition metal, in particular, the photocatalyst wherein a transition metal is platinum, further the photocatalyst for decomposition of water comprising any of these photocatalysts.

The Team:

A.Subrahmanyam
K.Jagadeesh Kumar
N.Jeevaraj

Dr.Paul Ramesh
Dr Jayasree Gopal
Dr. Revathy

Thanks for your Attention and Time