Rapid accelerated Hemodialysis in Children with End Stage renal Disease,

randomized clinical trial on its anticoagulant role and effects on the efficiency

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Mohamed Khaled El Hatw (MD),

Fatina Fadel (MD)

Ramzy El Baroudy (MD)

Introduction

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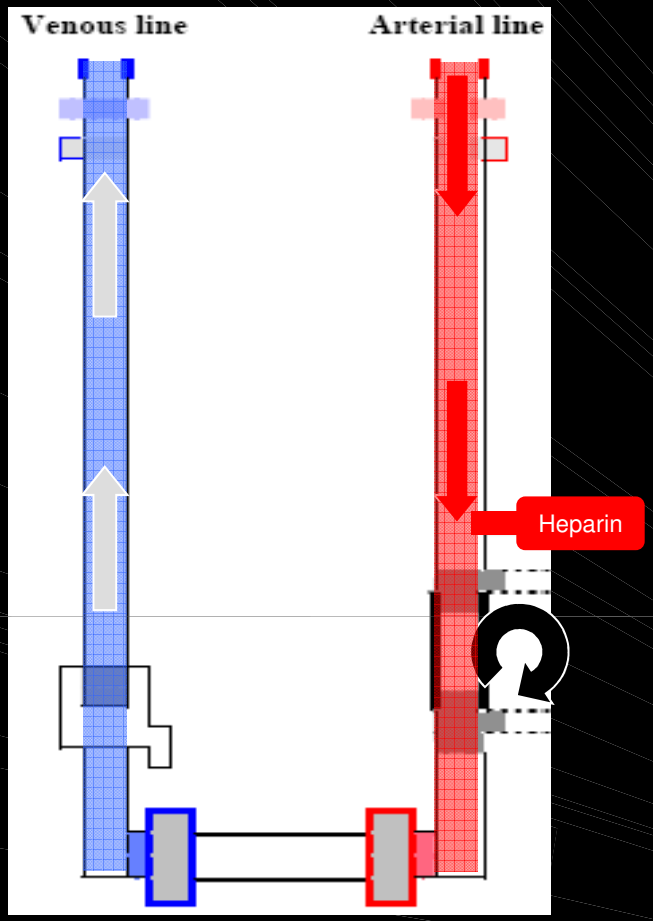
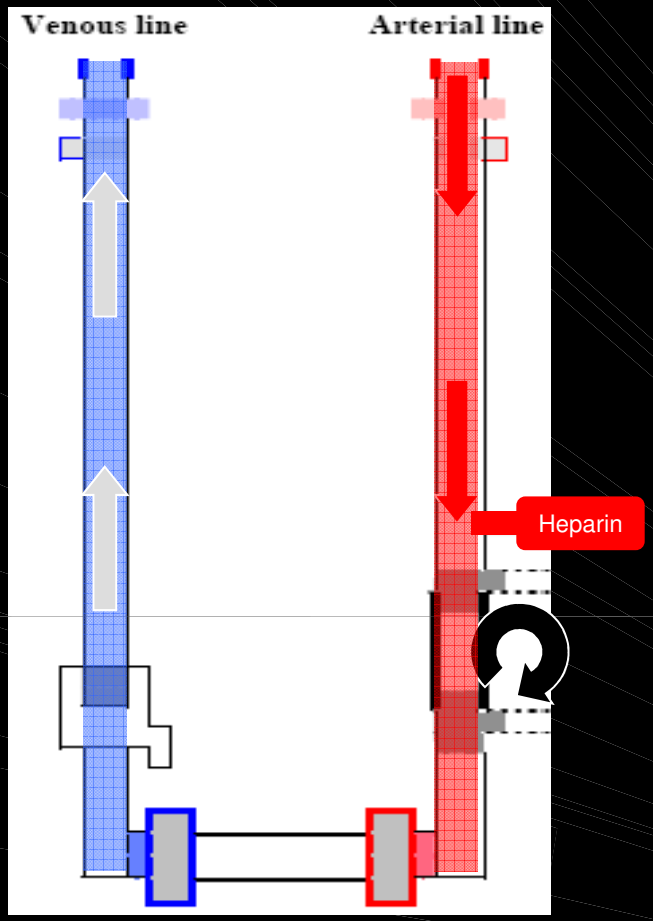


Routine heparin DNHD.

Increasing the blood flow rate (BFR) is a recommended strategy to improve efficiency of hemodialysis and to prevent blood clotting.

Rapid BFR “low dose heparin” and "no heparin" hemodialysis can achieve anticoagulation with low risk of anticoagulants induced bleeding, especially in patients with bleeding tendency. [1,2]

Introduction

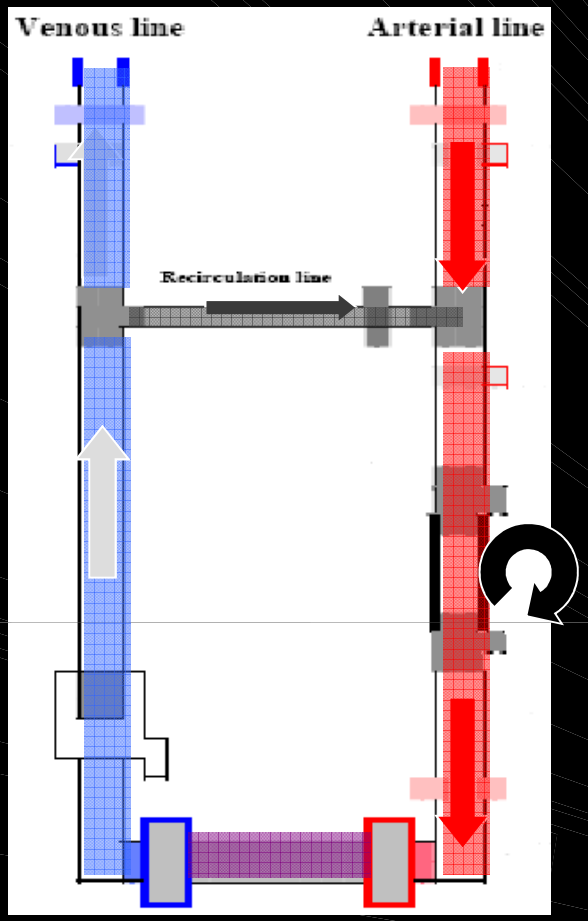


Routine heparin DNHD.

Without increasing the BFR, system coagulation occurred in no heparin dialysis in 13 of 296 (4 %) adults [3] - and in 7 out of 28 (25 %) children. [4]

Increasing the BFR carries the risk of heart failure and hypotension, especially in children, which might result in the interruption of treatment [1]

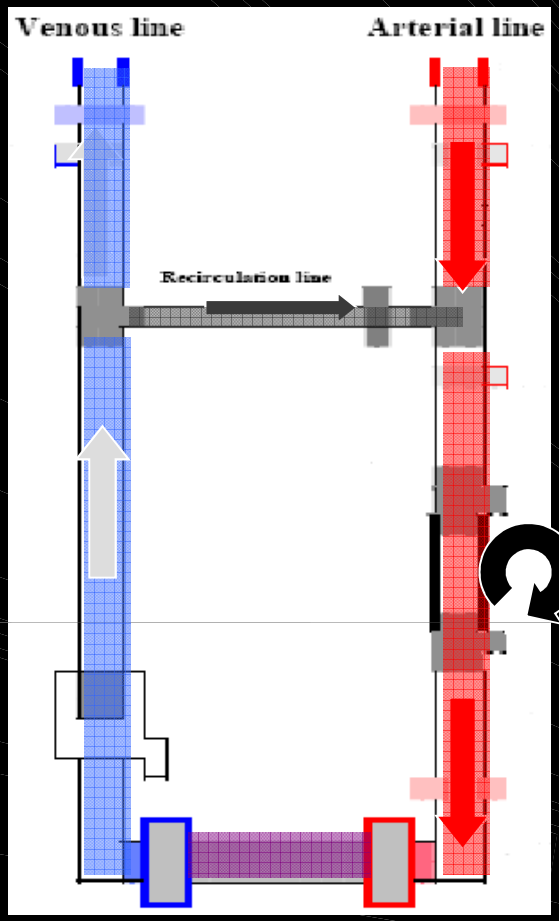
Introduction



AHD

Accelerated hemodialysis (AHD) is a hemodialysis technique where partial blood recirculation is used to selectively accelerate the BFR in the filter compared to the patient BFR

Introduction



Routine BFR

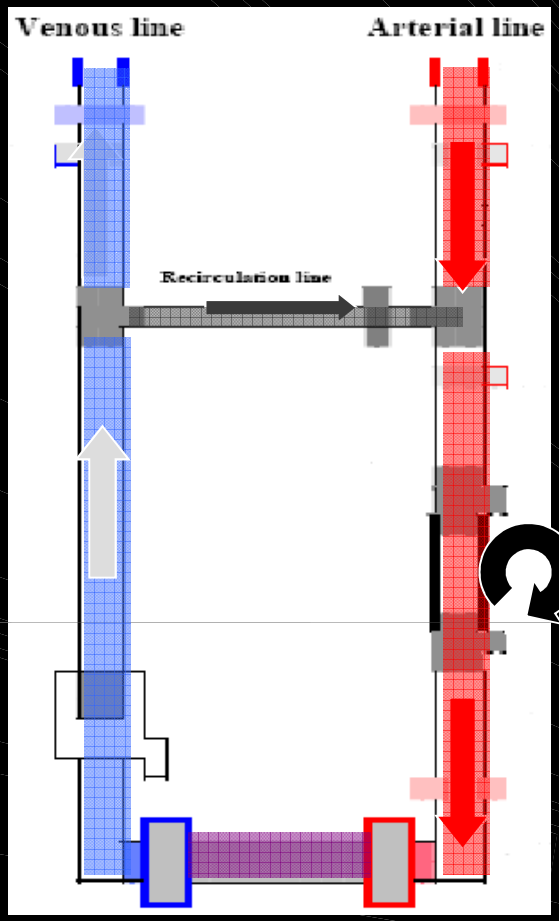
Selective Increase

R - AHD

Rapid accelerated hemodialysis (R-AHD) indicates that partial recirculation selectively increases the filter BFR.

PBR was reported by (1) Emura et al. 1985 cited in Yuji, 2008 [5] in hemodialysis sessions to achieve low-dose heparinization and by (2) El Hatw, 1999 [6] in 10 R-AHD sessions.

Introduction



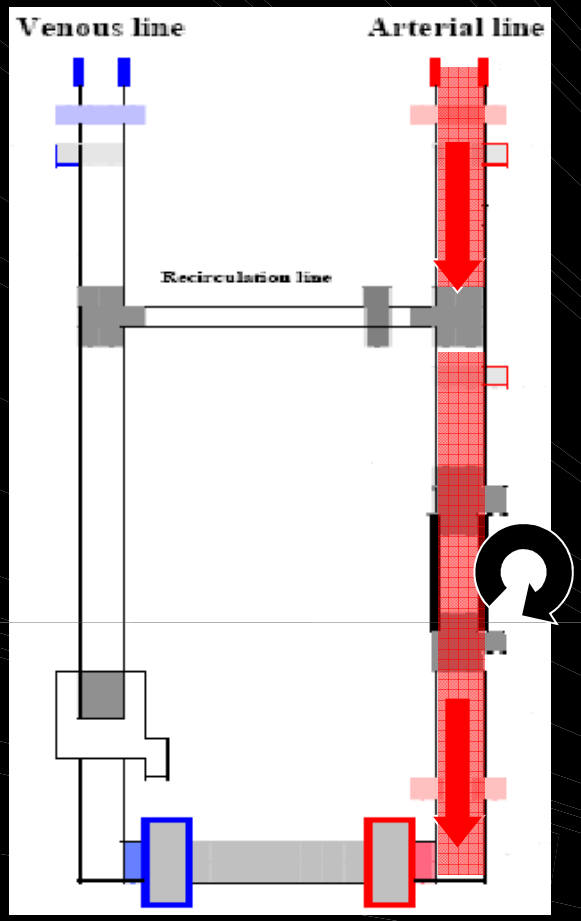
Selective Decrease

Routine BFR

S - AHD

Slow accelerated hemodialysis (S-AHD) indicates selective reduction of the patient BFR. It was reported by (1) Brendolan et al, 1994 cited in (Yuji, 2008) [5,] who called it "double pass hemodialysis". (2) El Hatw, in 1999[6] reported five S-AHD sessions for one patient with a patient BFR of 65 ml/minute and a recirculation BFR of 65 ml/ minute and (3) El Hatw et al [7] reported in 2007 65 Long S-AHD sessions, 8 hours each, for 5 patients and lastly (4) Yuji in 2008 [5] reported a case of continuous hemodiafilteration (CHDF) with unstable patient BFR and a recirculation BFR of 30 ml/ minute.

Introduction

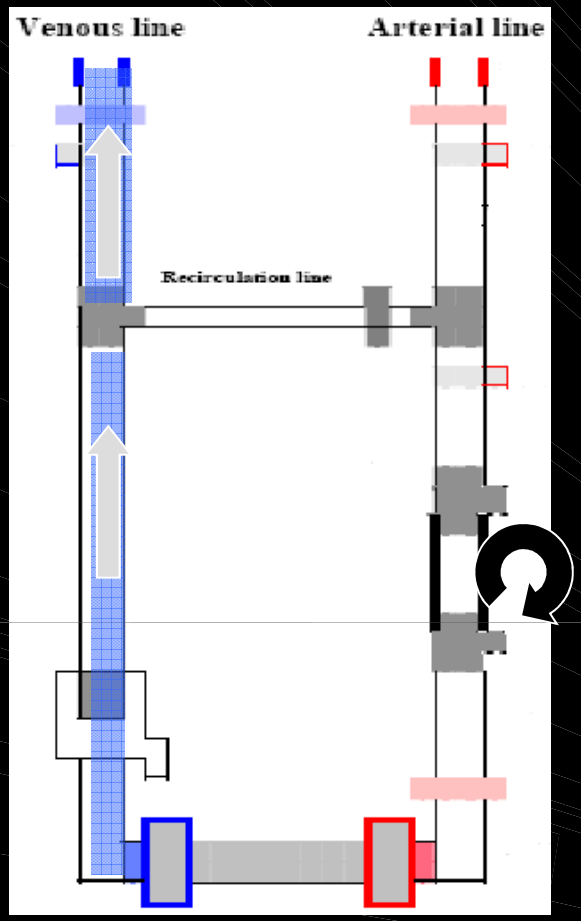


AHD Connections

AHD is carried out through H shaped AHD connections.

1. The 2 vertical lines of the “H” are the inflow (arterial) blood line that drains blood from the vascular access to the dialyser, and the outflow (venous) blood line that returns blood from the dialyser back to the vascular access [10].

Introduction



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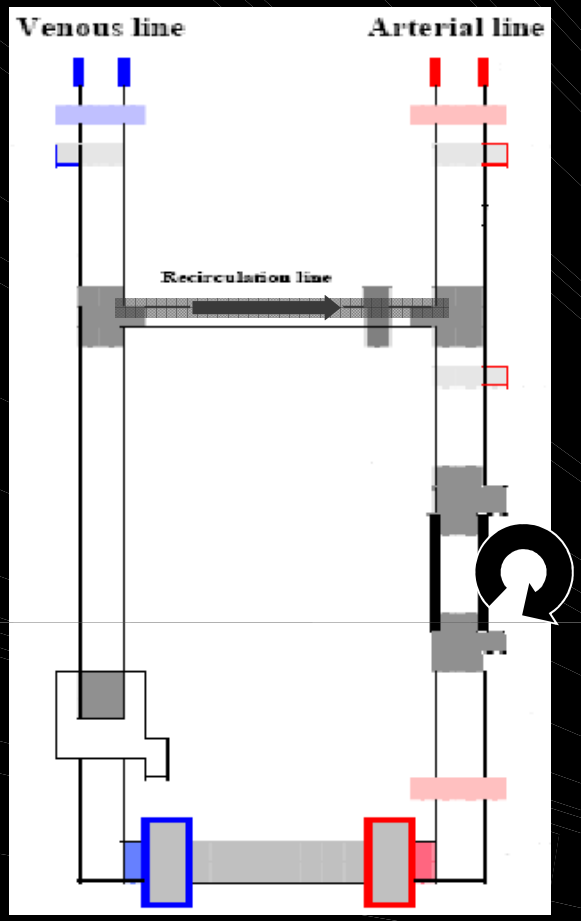
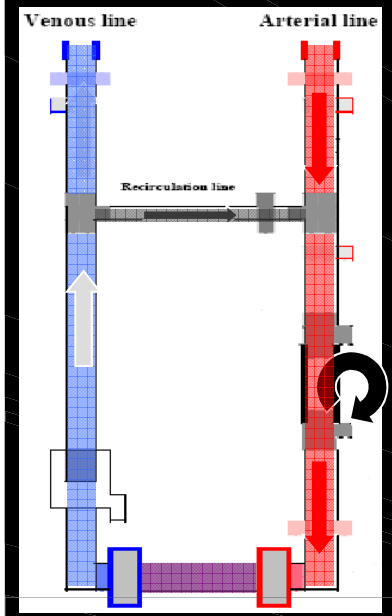


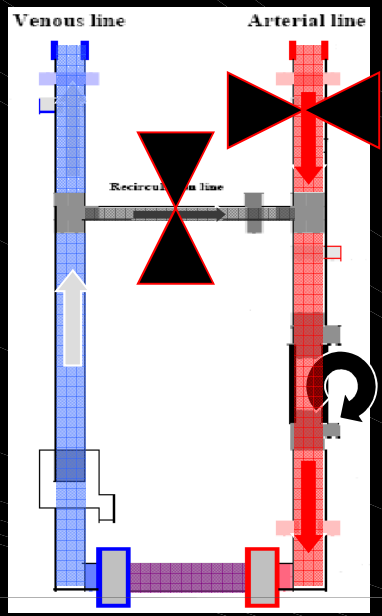
AHD Connections

(2) The recirculation line (R) forms the transverse limb of the H and divides the arterial line into the filter segment (F^a) and the patient segment (P^a) of the arterial line and divides the venous line into the filter segment (F^v) and the patient segment (P^v) of the venous line.

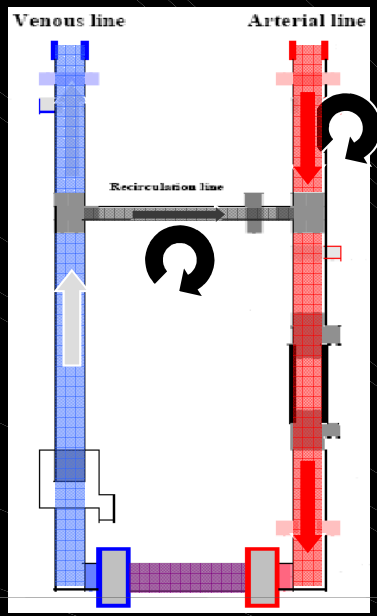
Introduction



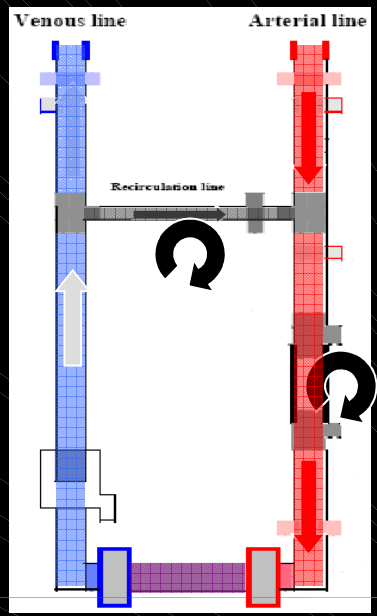
AHD^{0} Connections



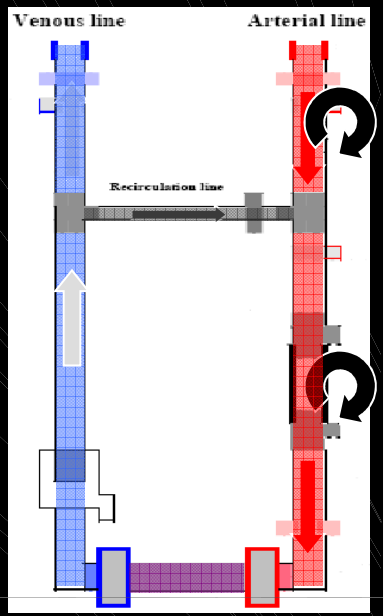
AHD^{V} Connections



AHD^{PR} Connections



AHD^{FR} Connections



AHD^{FP} Connections

AHD connections are available in 5 models; named according to the mode of control BFR of its different parts.

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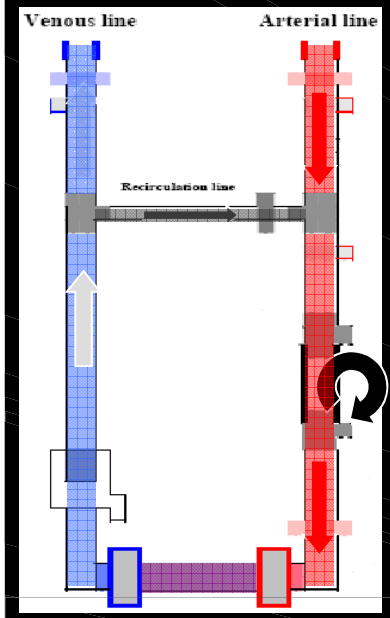
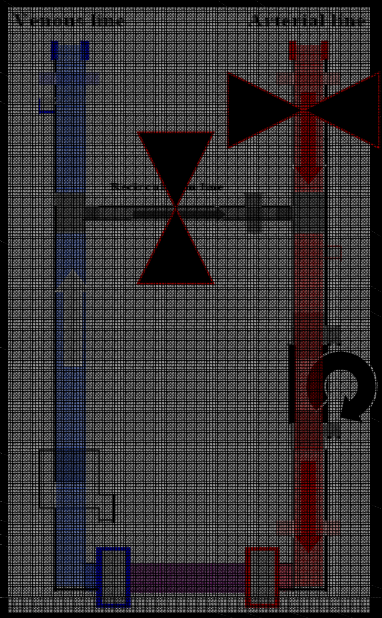
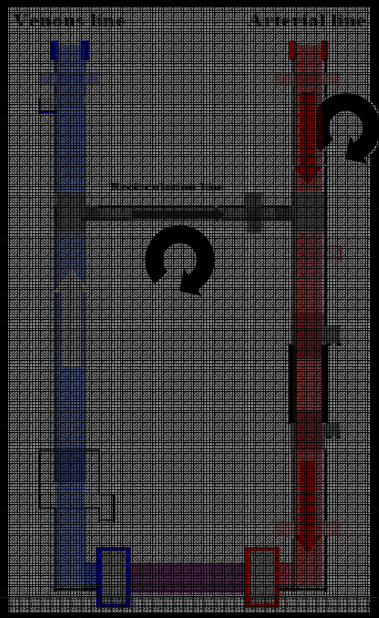


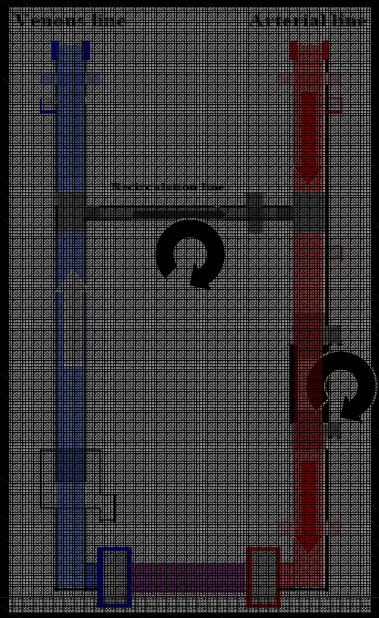
AHD^{0} Connections



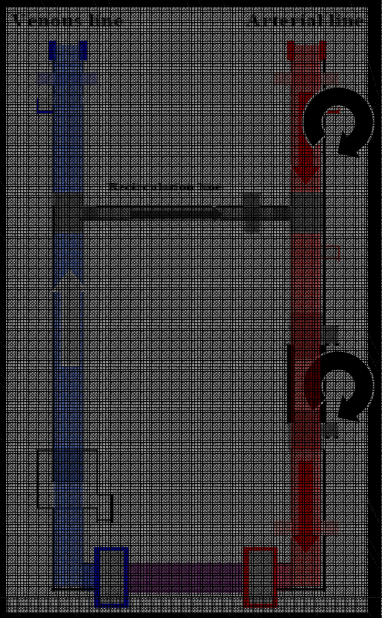
AHD^{V} Connections



AHD^{PR} Connections



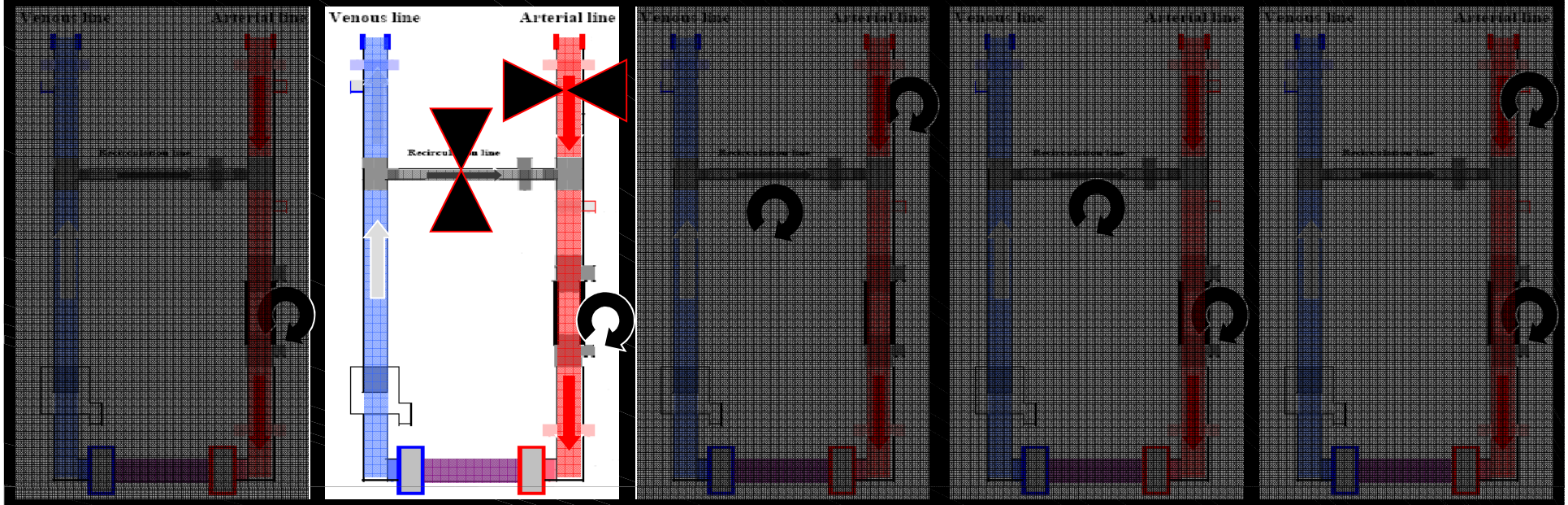
AHD^{FR} Connections



AHD^{FP} Connections

Model AHD^{0} has a single blood pump the filter portion of the arterial line (F^{a})

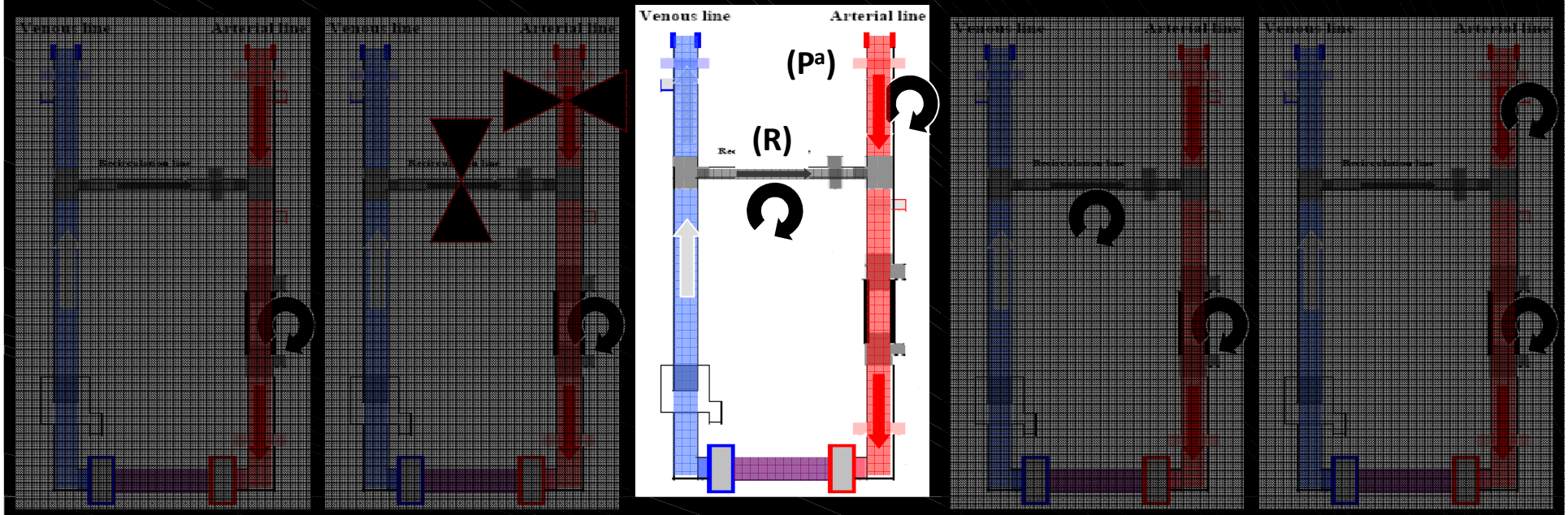
Introduction



AHD^{0} Connections | AHD^{V} Connections | AHD^{PR} Connections | AHD^{FR} Connections | AHD^{FP} Connections

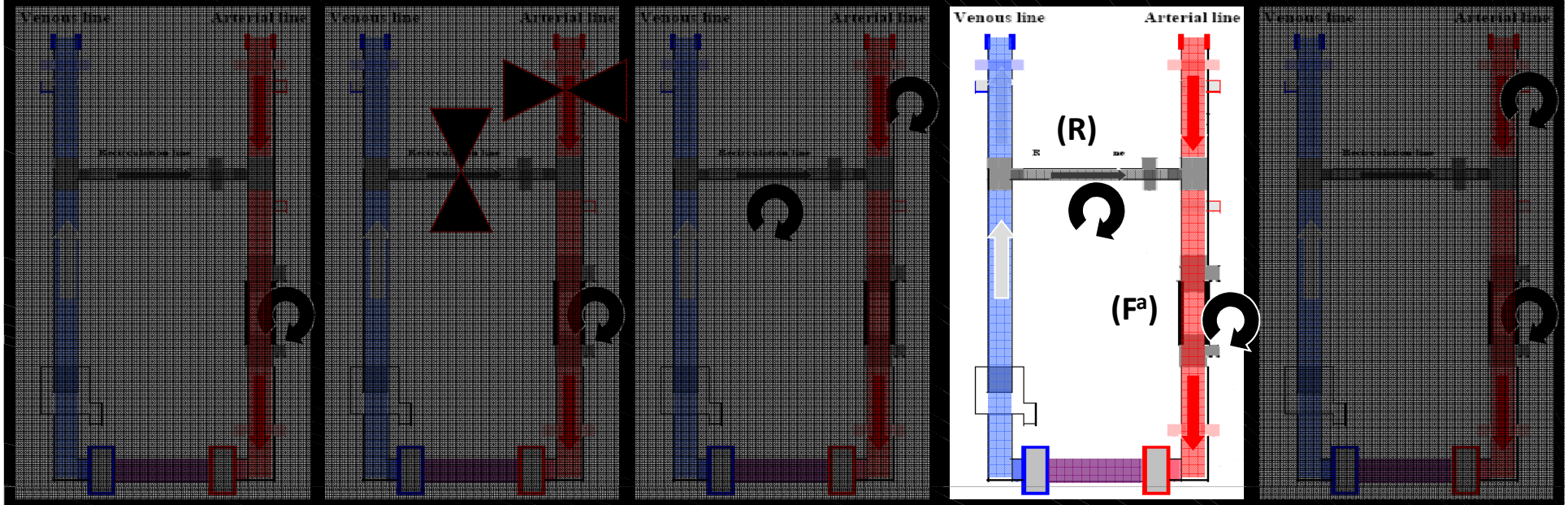
Model AHD^{V} has a single blood pump segment at the filter portion of the arterial line (F^{a}) in addition to 2 valves at the recirculation line (R) and the patient segment of the arterial line (P^{a})

Introduction



Model AHD^{PR} has one pump at Patient segment of arterial line (P^a) & the second at the recirculation line (R)

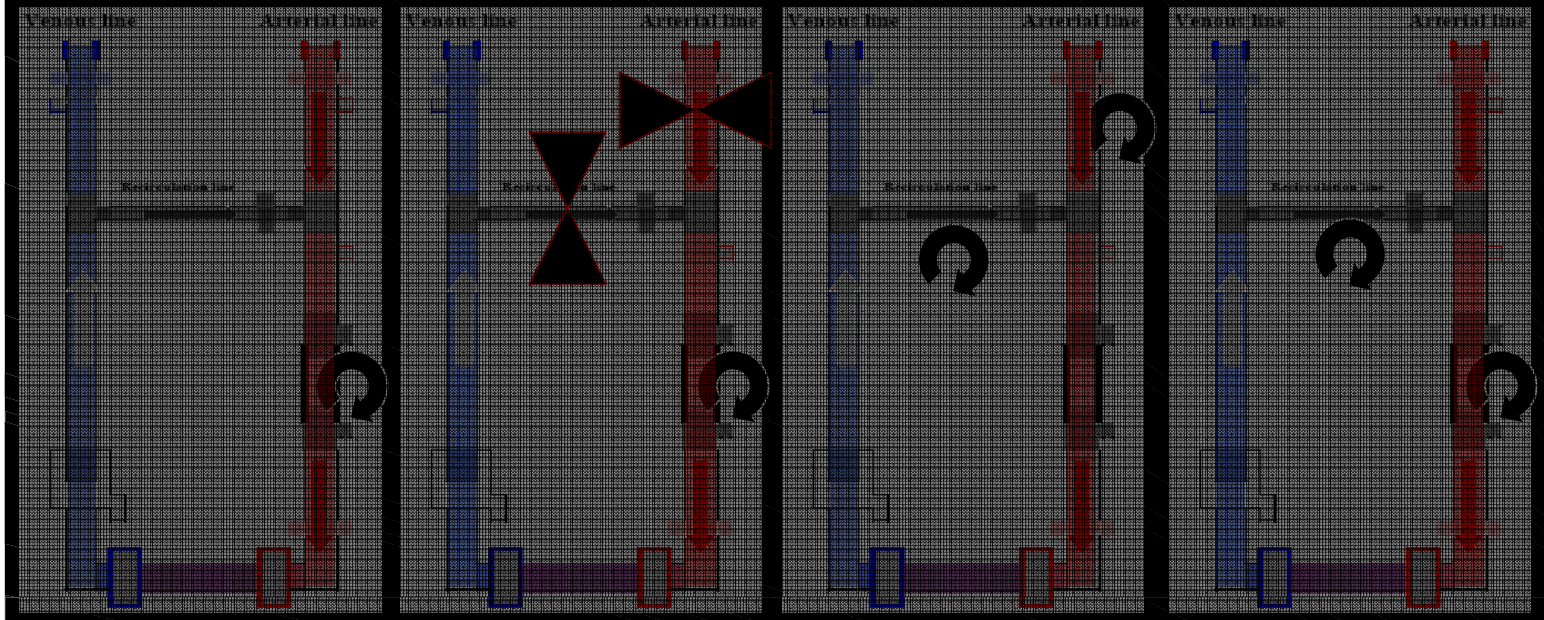
Introduction



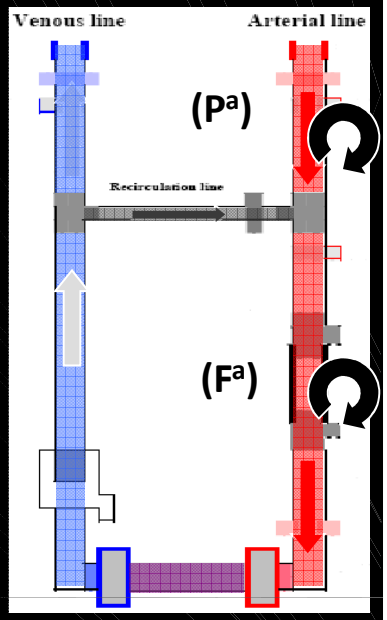
AHD^{0} Connections AHD^{V} Connections AHD^{PR} Connections **AHD^{FR} Connections** AHD^{FP} Connections

Model AHD^{FR} has one pump at Filter segment of arterial line (F^a) & the second at the recirculation line (R)

Introduction



AHD^{D} Connections AHD^{V} Connections AHD^{PR} Connections AHD^{FR} Connections

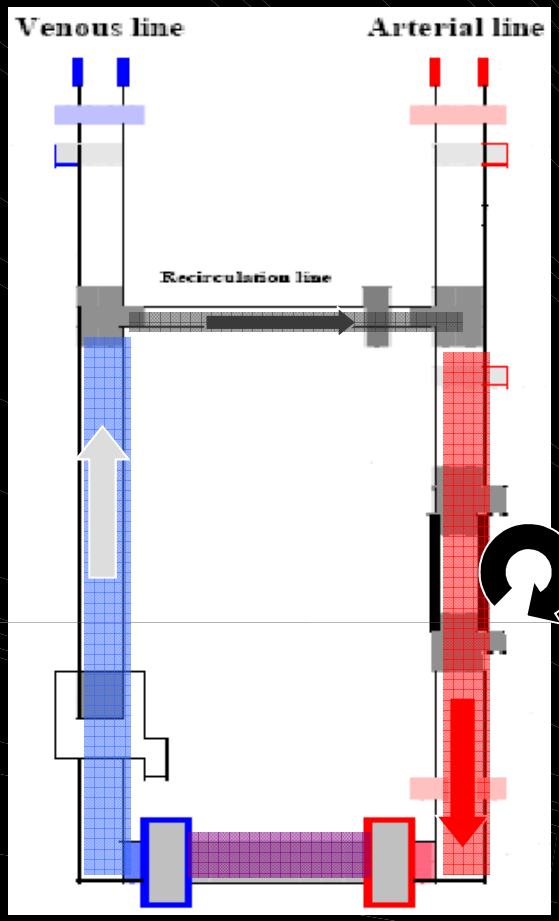


AHD^{FP} Connections

Model AHD^{FP} has one pump at Filter segment of arterial line (F^a) & the second at the Patient segment of the arterial line (P^a)

Introduction

(Pᵛ)



(Pᵃ)

Closed Circuit AHD

Closing the patient segment of the arterial line (Pᵃ) and of the venous line (Pᵛ) clamps during the AHD session will create a closed circuit involving the (R), (Fᵃ), the filter and (Fᵛ) and allow adjustment of the bypassed fistula needles by the operator.

Introduction

جمهورية مصر العربية
وزارة الدولة لشئون البحث العلمى

أكاديمية البحث العلمى والتكنولوجيا

براءة اختراع
رقم ٢١٥٨٧

رئيس أكاديمية البحث العلمي و التكنولوجيا

بعد الاطلاع علي المادة ٢٤ من القانون رقم ١٣٢ لسنة ١٩٤٩ الخاص ببراءات الاختراع و الرسوم و النماذج الصناعية ،وعلي قرار رئيس الجمهورية رقم ٣٧٧ لسنة ١٩٩٨ بتولي أكاديمية البحث العلمى و التكنولوجيا الاختصاصات المنصوص عليها في القانون المشار إليه فيما يتعلق ببراءات الاختراع .
وعلي طلب البراءة رقم ٥٤٧ في ٢٠ من شهر مايو سنة ١٩٩٨ والمستندات الملحقة به

مادة ١ تمنح براءة اختراع أصلية برقم : ٢١٥٨٧
إلى : الدكتور /محمد خالد محمد عبد المعطى الحتو •
المركز العام : ٥٢ شارع محمود شلتوت – امتداد الطيران – أمام مستشفى التأمين الصحي – مدينة نصر – القاهرة – جمهورية مصر العربية •
عن اختراع : وصلات لسرعة الغسيل الدموى •
اسم المخترع : ----------
مدة البراءة : عشرون عاما تبدأ من يوم٢٠ مايو ١٩٩٨وتنتهى فى يوم ١٩ مايو ٢٠١٨
وقد توضح بيانه في الوصف المرفق بهذا القرار

ويتمتع الطلب بحق أسبقية استنادا للطلب رقم لايوجد المودع ------- بتاريخ ----------

مادة ٢ صدر هذا القرار في القاهرة يوم ٣١ ديسمبر ٢٠٠١

مادة ٣ علي الجهة المختصة نشره في جريدة براءات الاختراع

لايعنىمنح هذه البراءة إعطاء الحق بتسويق المنتج داخل جمهورية مصر العربية ، ولتسويق المنتج موضوع هذه البراءة يلزم اتباع الإجراءات والقواعد القانونية المعمول بها للحصول على حق التسويق والتداول داخل جمهورية مصر العربية من الوزارات المعنية

رئيس
أكاديمية البحث العلمى و التكنولوجيا

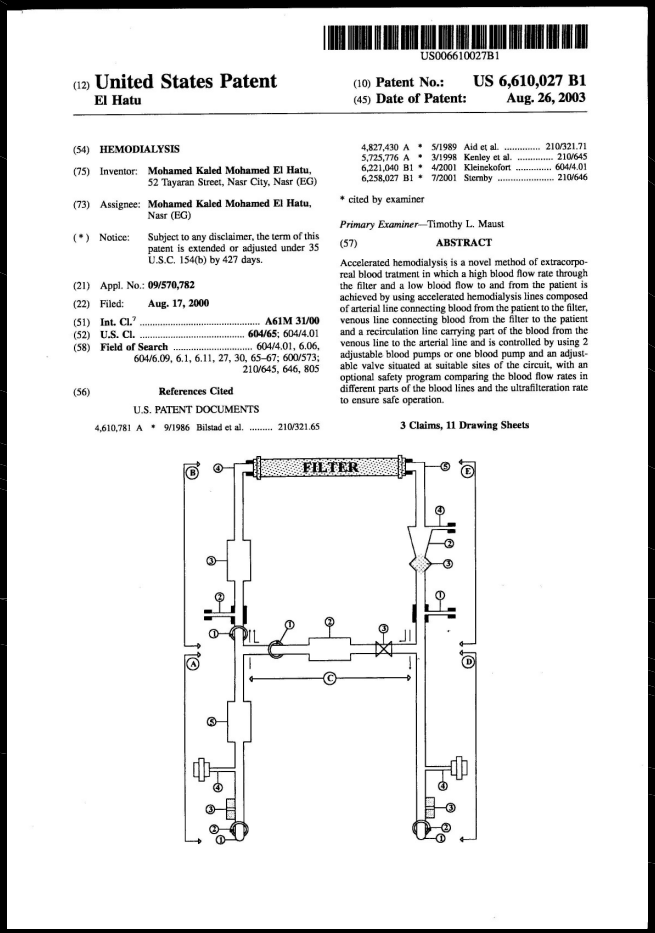
نائب رئيس الأكاديمية
للتنمية التكنولوجية والخدمات العلمية

رئيس مكتب براءات الاختراع

Patent no. 21587 **Egyptian patent office**

The AHD connections are registered inventions by El hatw in the Egyptian patent office [8] and the USA patent office [9].

Introduction



US006610027B1

(12) **United States Patent**
El Hatu

(10) **Patent No.: US 6,610,027 B1**
(45) **Date of Patent: Aug. 26, 2003**

(54) **HEMODIALYSIS**

(75) Inventor: **Mohamed Kaled Mohamed El Hatu**, 52 Tayaran Street, Nasr City, Nasr (EG)

(73) Assignee: **Mohamed Kaled Mohamed El Hatu**, Nasr (EG)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 427 days.

(21) Appl. No.: **09/570,782**

(22) Filed: **Aug. 17, 2000**

(51) **Int. Cl.**[7] **A61M 31/00**

(52) **U.S. Cl.** **604/65**; 604/4.01

(58) **Field of Search** 604/4.01, 6.06, 604/6.09, 6.11, 27, 30, 65–67; 600/573; 210/645, 646, 805

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* cited by examiner

Primary Examiner—Timothy L. Maust

(57) **ABSTRACT**

Accelerated hemodialysis is a novel method of extracorporeal blood tratment in which a high blood flow rate through the filter and a low blood flow to and from the patient is achieved by using accelerated hemodialysis lines composed of arterial line connecting blood from the patient to the filter, venous line connecting blood from the filter to the patient and a recirculation line carrying part of the blood from the venous line to the arterial line and is controlled by using 2 adjustable blood pumps or one blood pump and an adjustable valve situated at suitable sites of the circuit, with an optional safety program comparing the blood flow rates in different parts of the blood lines and the ultrafilteration rate to ensure safe operation.

3 Claims, 11 Drawing Sheets

The United States of America

The Director of the United States Patent and Trademark Office

Has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this

United States Patent

Grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America for the term set forth below, subject to the payment of maintenance fees as provided by law.

If this application was filed prior to June 8, 1995, the term of this patent is the longer of seventeen years from the date of grant of this patent or twenty years from the earliest effective U.S. filing date of the application, subject to any statutory extension.

If this application was filed on or after June 8, 1995, the term of this patent is twenty years from the U.S. filing date, subject to any statutory extension. If the application contains a specific reference to an earlier filed application or applications under 35 U.S.C. 120, 121 or 365(c), the term of the patent is twenty years from the date on which the earliest application was filed, subject to any statutory extensions.

Director of the United States Patent and Trademark Office

Patent no. 6610027

USPTO

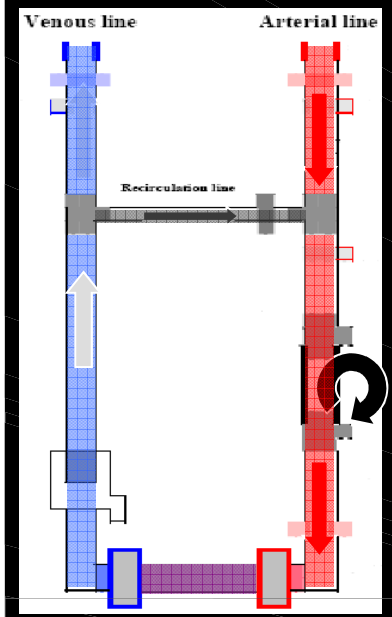
The AHD connections are registered inventions by El hatw in the Egyptian patent office [8] and the USA patent office [9].

Objectives

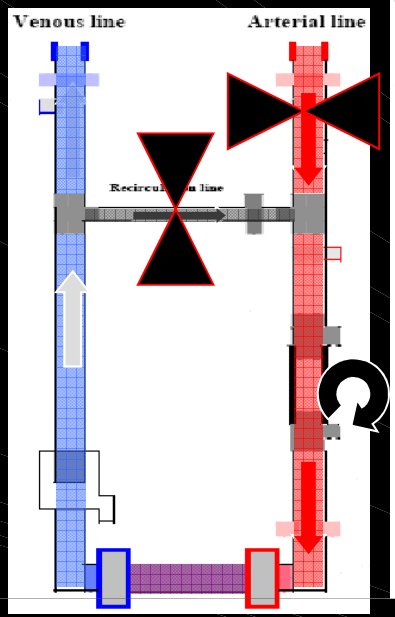
Objectives

Objectives: Assess R-AHD with regards to anticoagulation effect and effect on the dialysis efficiency.

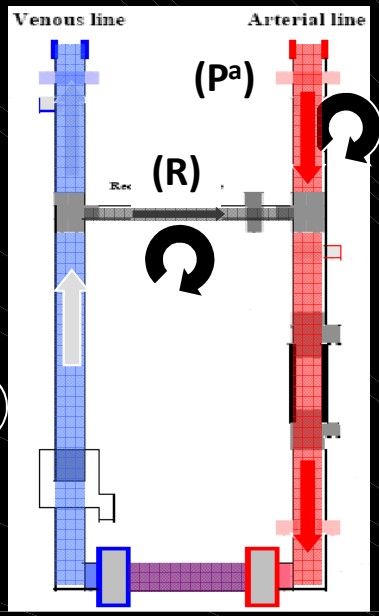
Objectives



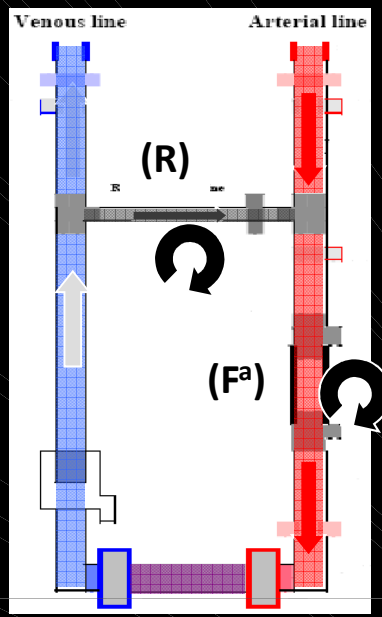
AHD^{0} Connections



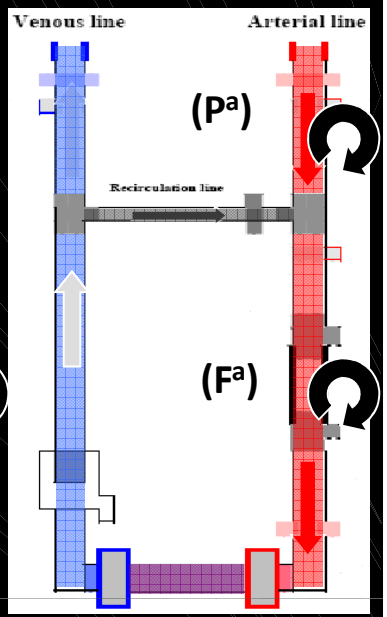
AHD^{V} Connections



AHD^{PR} Connections



AHD^{FR} Connections



AHD^{FP} Connections

The main objectives of this study were to

(1) Explore the 5 different models of AHD connections with regards to their ability to decrease the heparin dose during hemodialysis and their effect on the dialysis efficiency.

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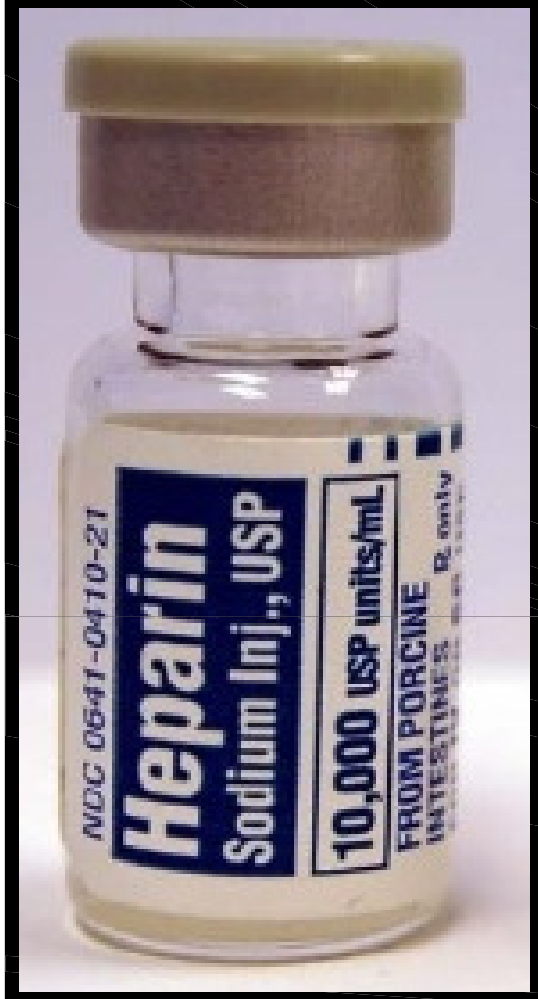

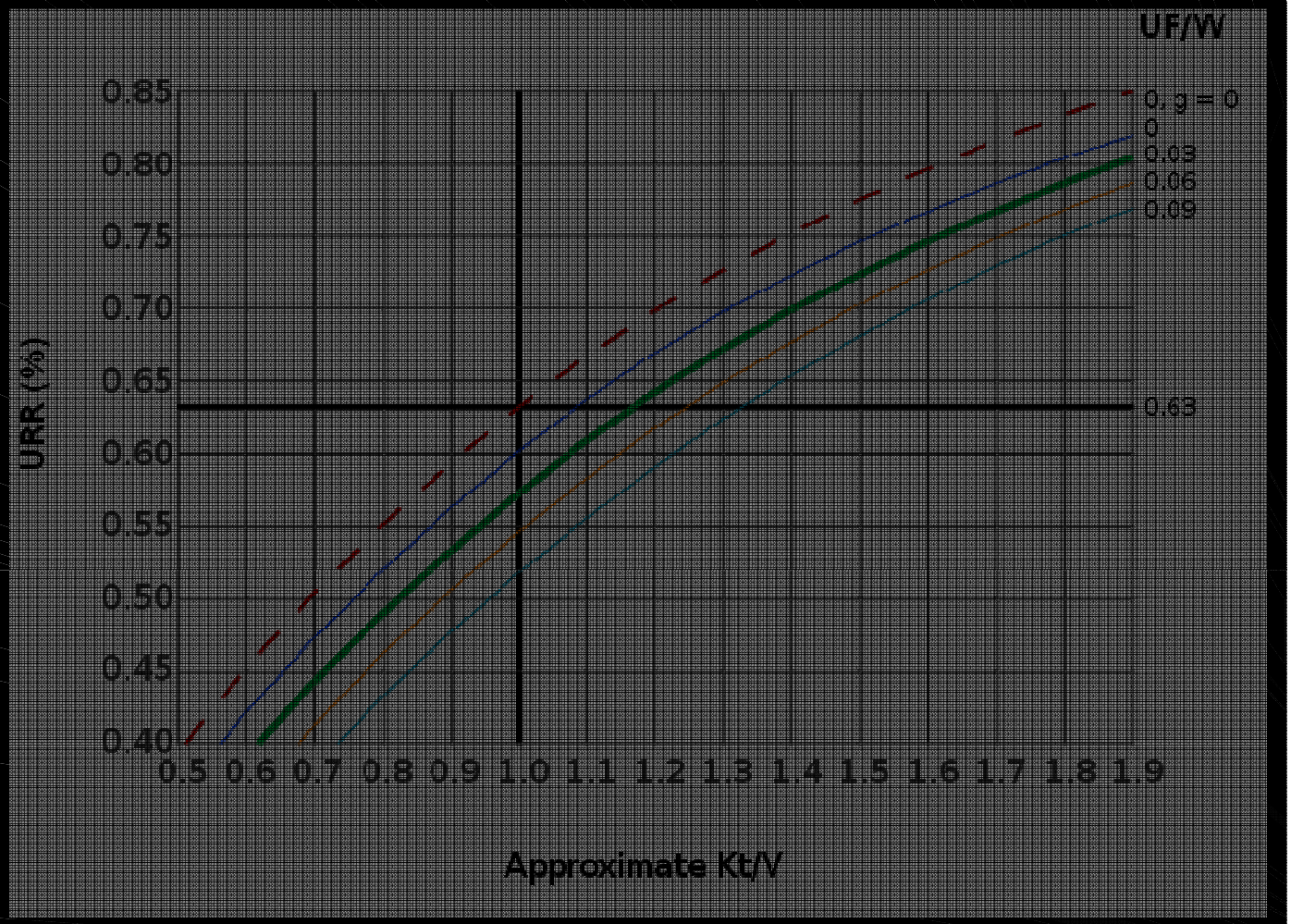

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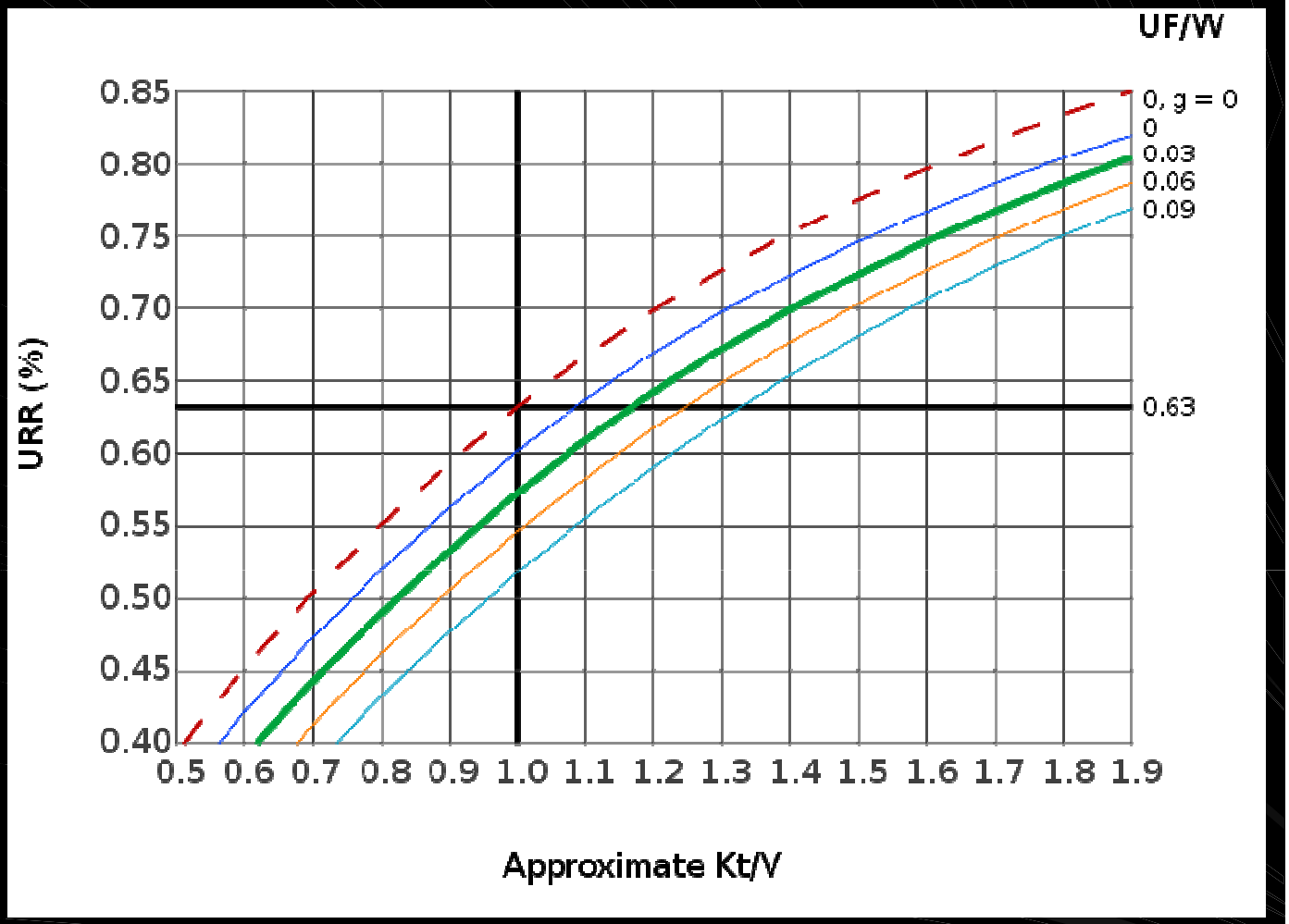

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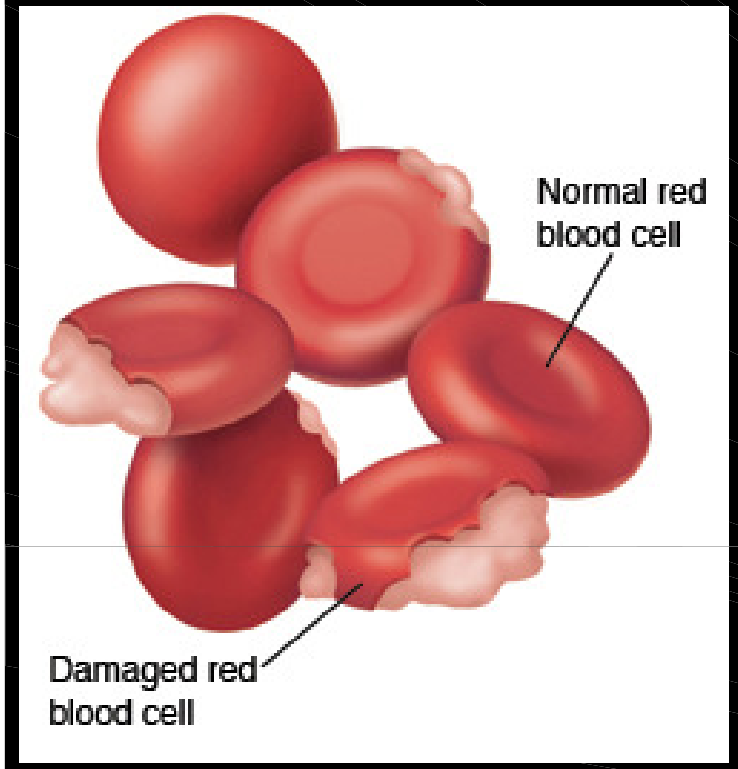
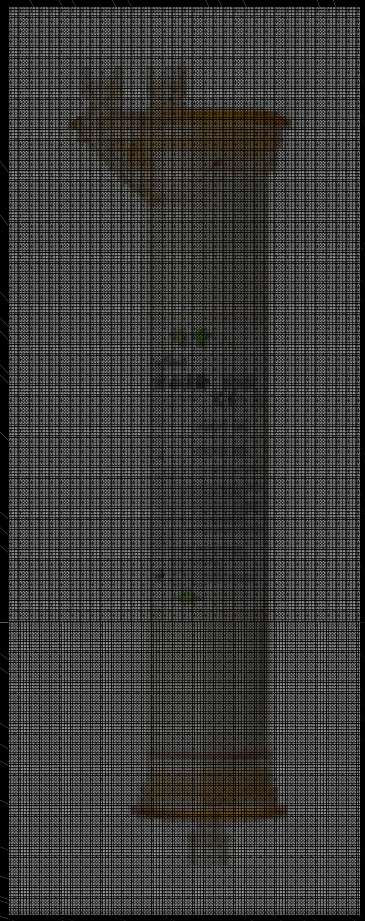
(1) Explore the 5 different models of AHD connections with regards to their ability to decrease the heparin dose during hemodialysis and their effect on the dialysis efficiency.

Objectives



RBCs Integrity

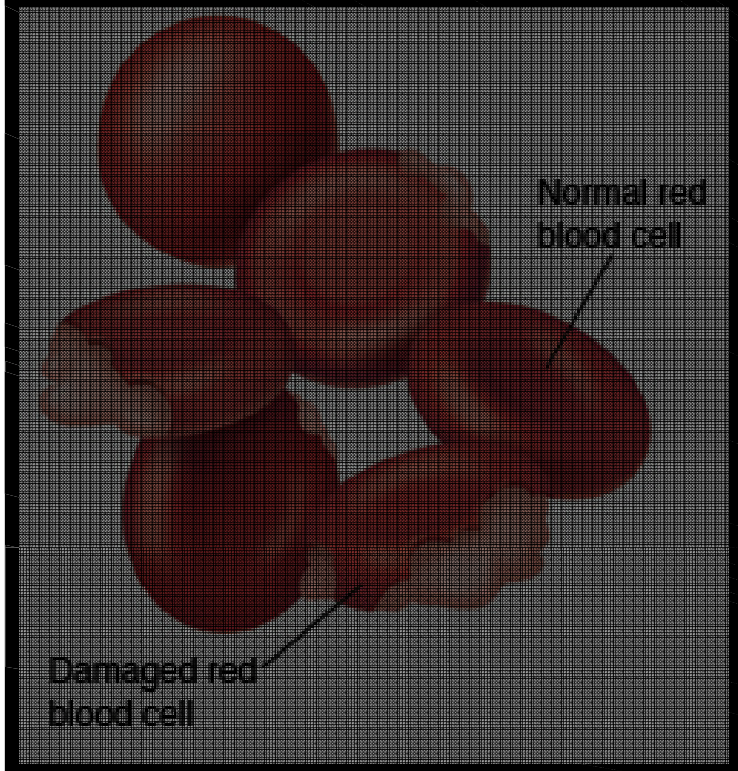
AV Fistula Integrity



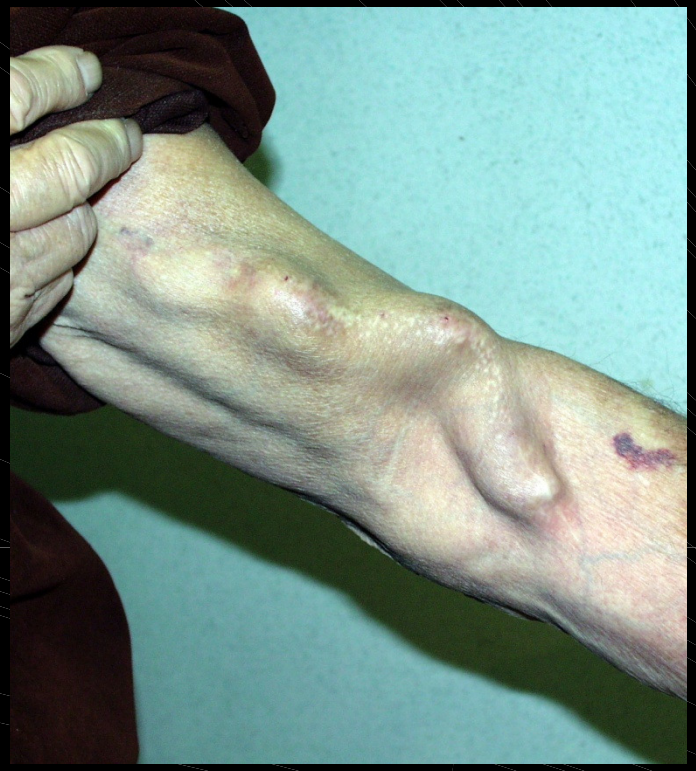
Hollow Fiber In

(2) Test safety of R-AHD on the integrity of the Red Blood Cells (RBCs), the arteriovenous (A-V) fistula and the hollow fibers of the filter.

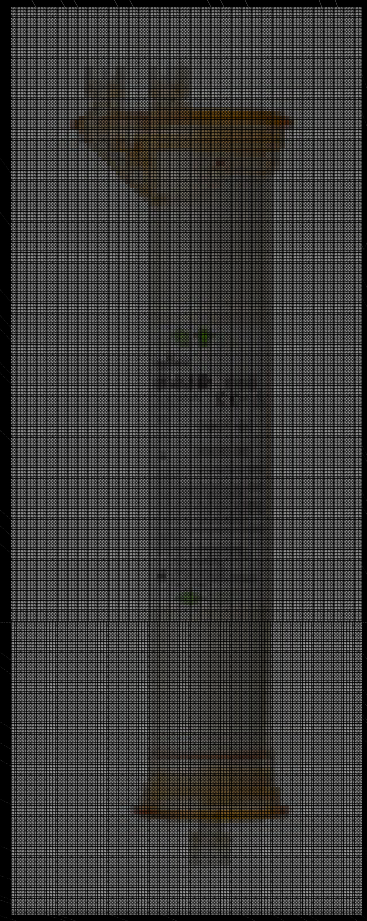
Objectives



RBCs Integrity



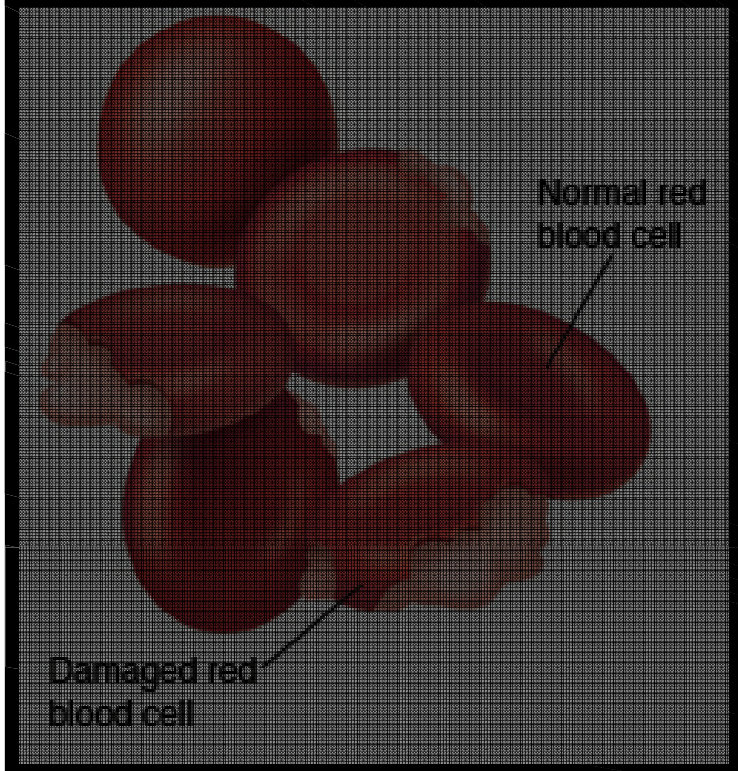
AV Fistula Integrity



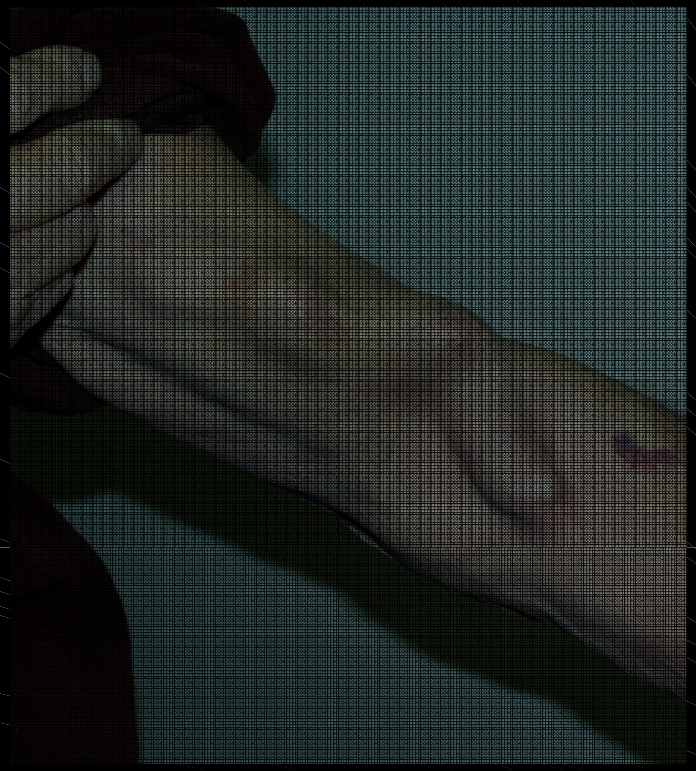
Hollow Fiber In

(2) Test safety of R-AHD on the integrity of the Red Blood Cells (RBCs), the arteriovenous (A-V) fistula and the hollow fibers of the filter.

Objectives



RBCs Integrity

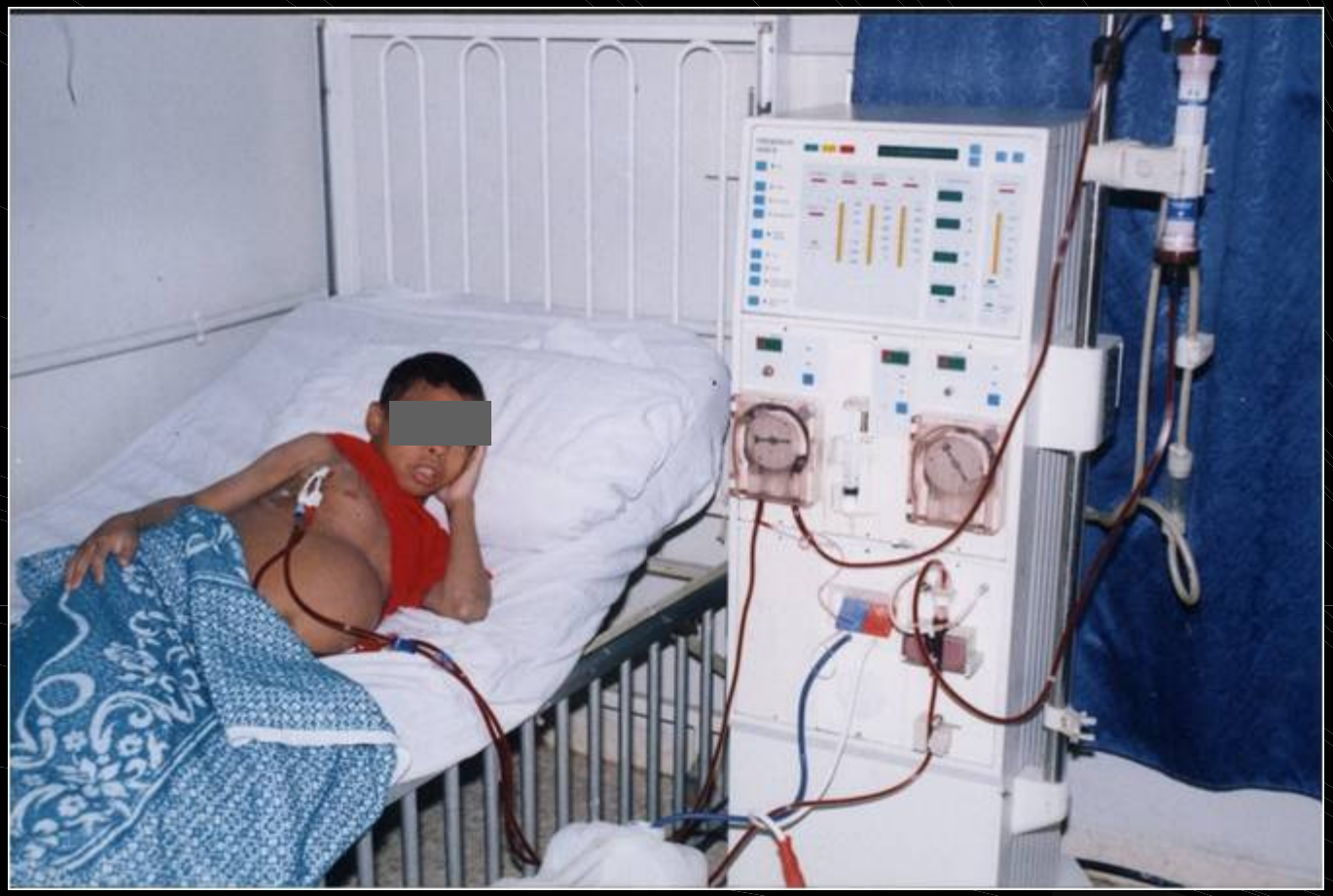


AV Fistula Integrity

Hollow Fiber In

(2) Test safety of R-AHD on the integrity of the Red Blood Cells (RBCs), the arteriovenous (A-V) fistula and the hollow fibers of the filter.

Objectives



Clinical Feasibility

(3) Assess the clinical feasibility of carrying out and maintaining children with end Stage renal disease (ESRD) on R-AHD.

PATIENTS & METHODS

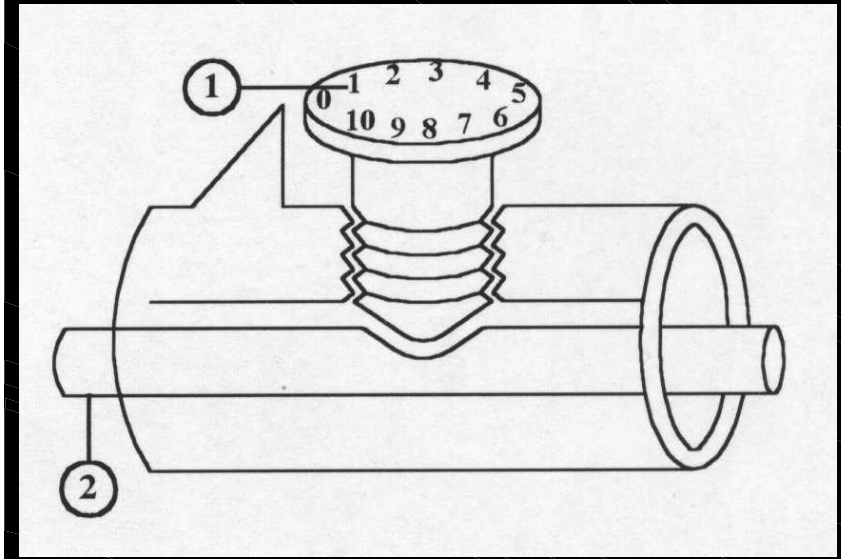
Methods - *Setting and Study design*

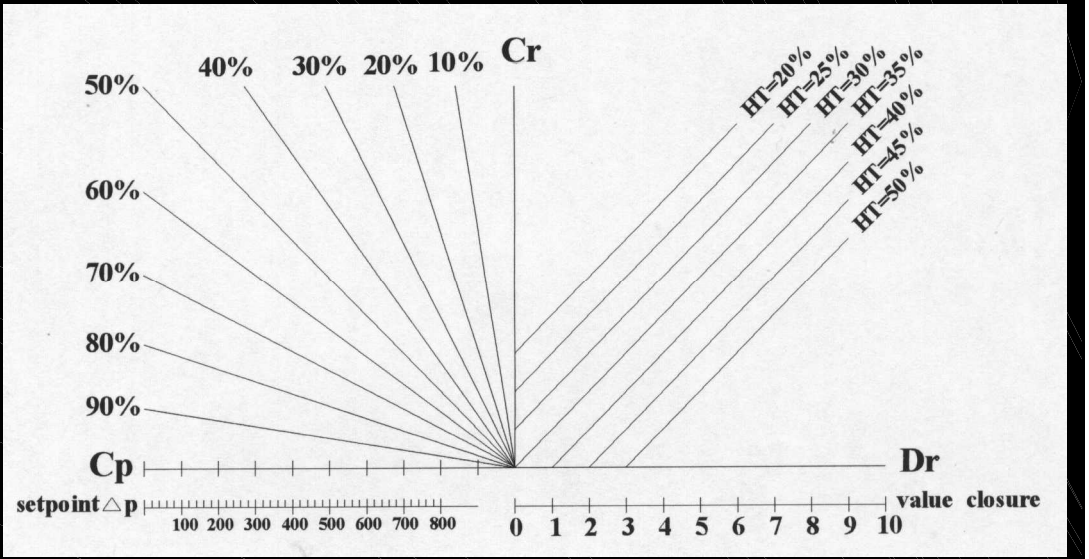
This study was carried out at Cairo University Children's Hospital, a quaternary referral urban hospital in Egypt. The hospital operates a hemodialysis unit with 25 hemodialysis machines.

Methods - *Setting and Study design*

The trial was part of a project to study “the outcomes of the invention AHD connections sponsored by the academy of Scientific Research, Egypt. where hydraulic and experimental studies preceded the clinical trial in addition to a clinical trial on S-AHD.

Methods - *Setting and Study design*





The hydraulic study of the project included calibration of the valve of AHD^{V} connections and development of a new instrument for measurement of the patient BFR in the (P^{a}) during AHD^{0} and AHD^{V} sessions called “air bubble speed”; whereby the patient BFR rate is estimated from the time needed for an air bubble injected at the injection site of (P^{a}) to reach the junction of (P^{a}) and (R).

Methods - *Setting and Study design*

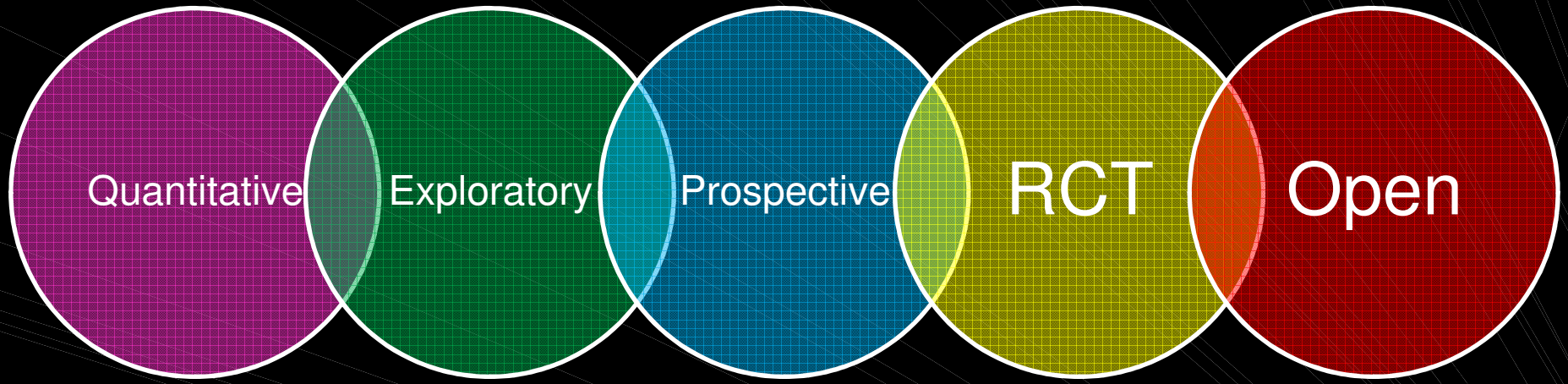
The proposal of the project was revised, modified and finally approved by

1. The scientific committee of the sponsoring governmental non profit organization "Academy of scientific research and technology" and by
2. The scientific committee of the pediatric department of Cairo University hospital where the trial was conducted.

Methods - *Setting and Study design*

The report of the project was disclosed, but not published, in 2006 [11] and the clinical trial on S-AHD was published in 2007[7].

Methods - *Setting and Study design*



The clinical trial was

(1) Quantitative

(2) Exploratory: It explored the feasibility, benefits & drawbacks of carrying R-AHD using 5 models of the invented AHD connections.

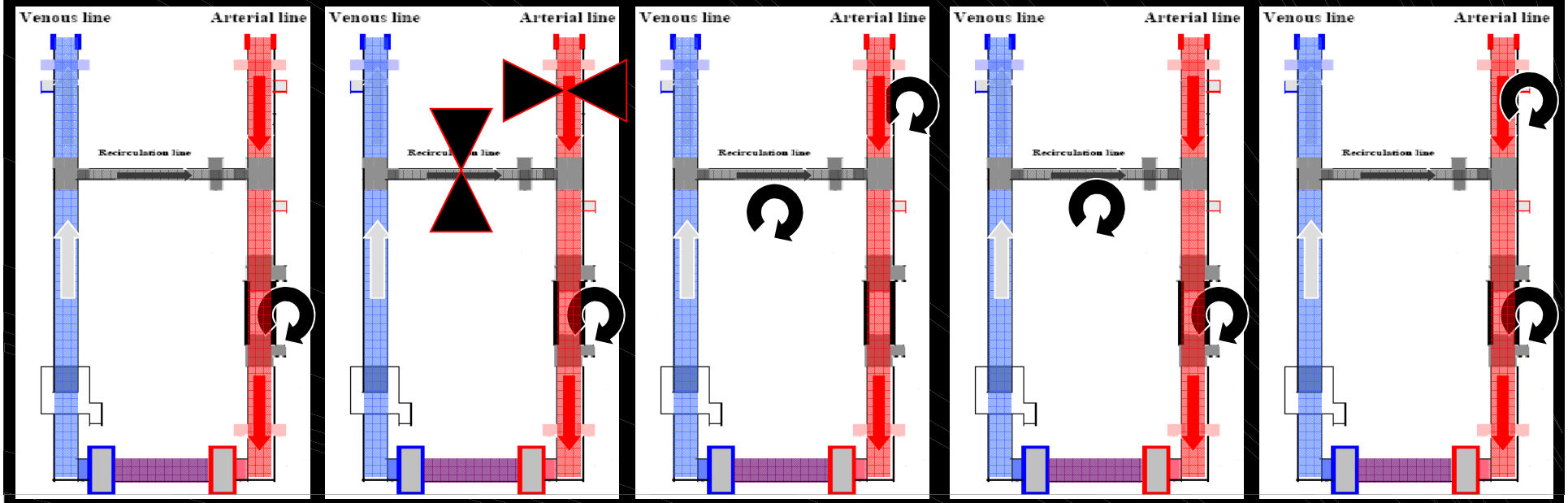
(3) Prospective

(4) Randomized, Controlled

(5) Open to the operators and to the patients as blinding the intervention was impossible but the blood tests were blindly assessed outcomes.

(6) The primary and secondary endpoints were objective.

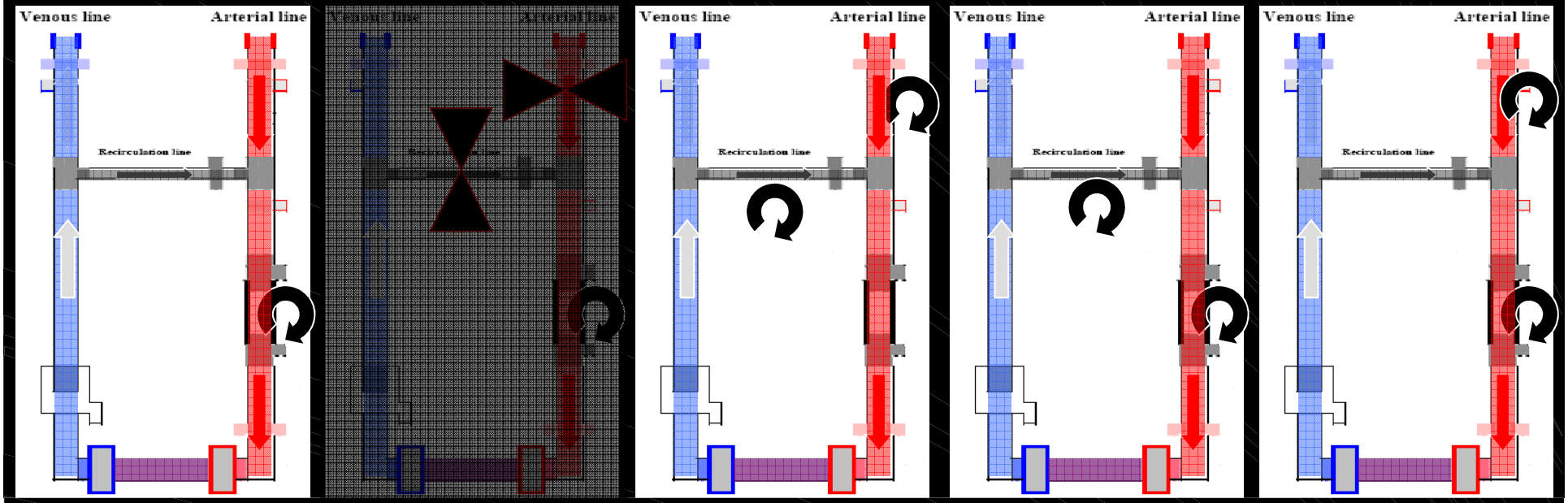
Methods - *Setting and Study design*



R - AHD^{0} R - AHD^{V} R - AHD^{PR} R - AHD^{FR} R – AHD^{FP}

Each Stage of the clinical trial was intended to study R-AHD, using one of the 5 models of AHD connections.

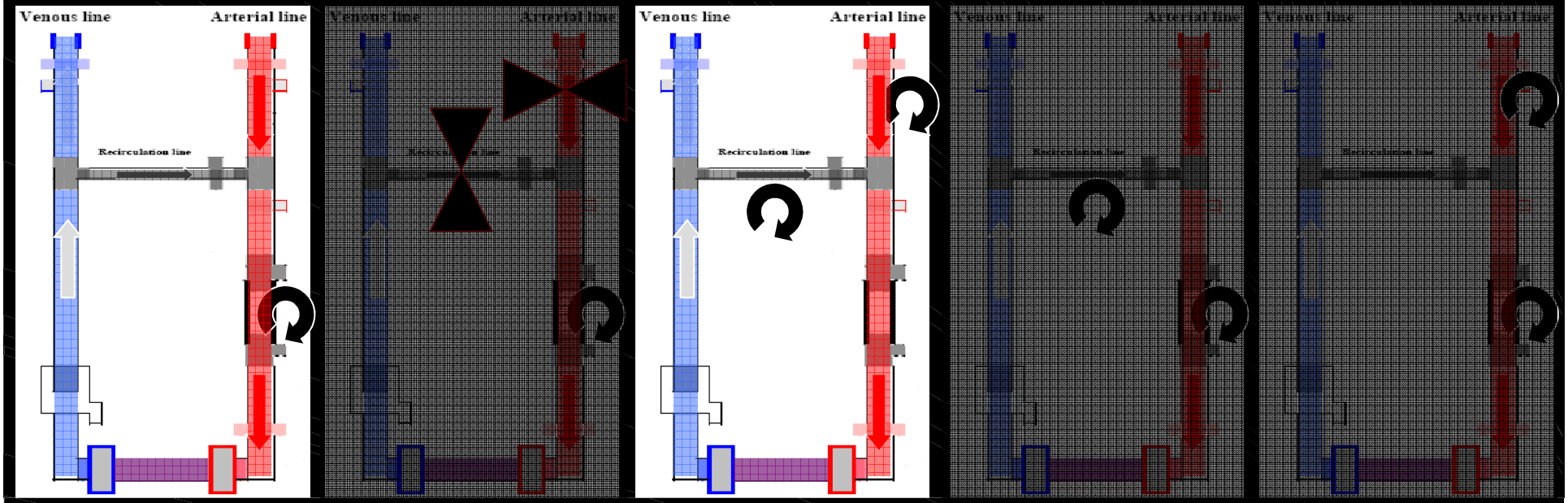
Methods - *Setting and Study design*



R - AHD^{0} R - AHD^{V} R - AHD^{PR} R - AHD^{FR} R – AHD^{FP}

1) R-AHD^{V} Stage was aborted due to difficulties in adjusting the manual valve in a clinical session

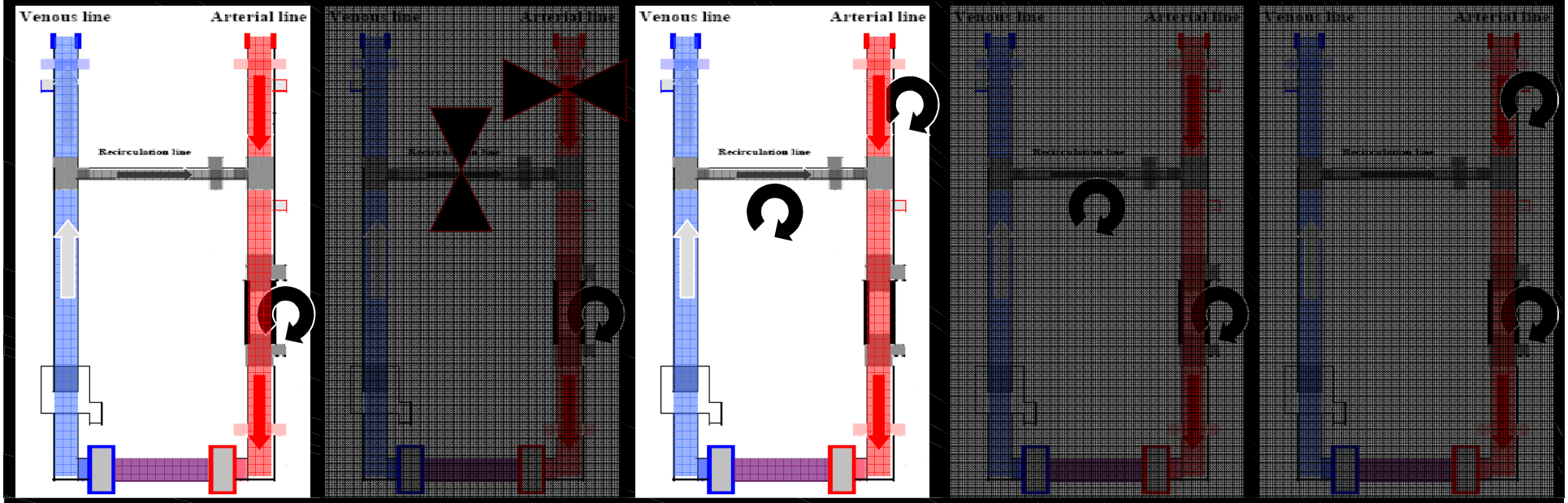
Methods - *Setting and Study design*



R - AHD^{0} R - AHD^{V} R - AHD^{PR} R - AHD^{FR} R – AHD^{FP}

(2) R-AHD^{FR} and the R-AHD^{FP} Stages were aborted due to a threat of air embolism as the blood pump attached to (F^{a}) while returning blood to the patient at the end of the session.

Methods - *Setting and Study design*

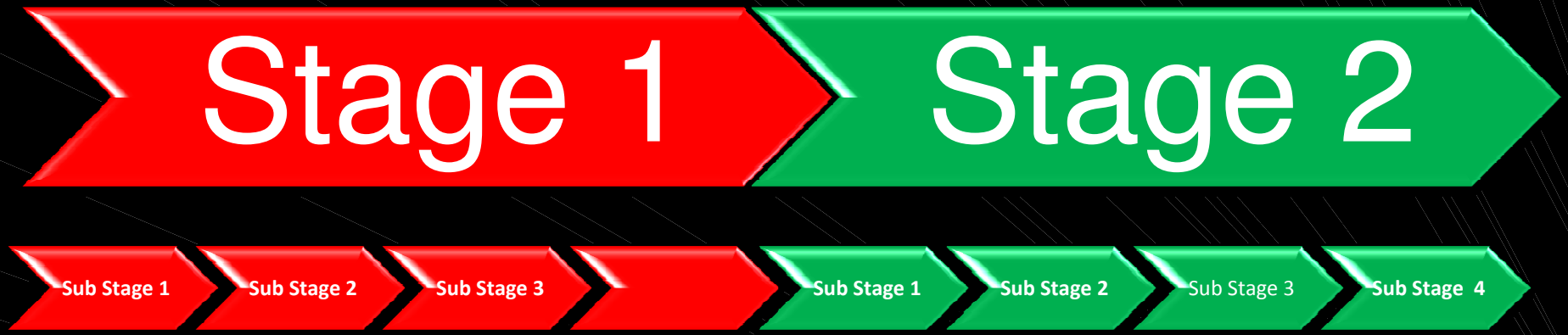


R - AHD^{0} R - AHD^{V} R - AHD^{PR} R - AHD^{FR} R - AHD^{FP}

Two AHD models were ultimately studied

- R-AHD^{0} sessions in **Stage 1** and
- R-AHD^{PR} sessions in **Stage 2**.

Methods - *Setting and Study design*



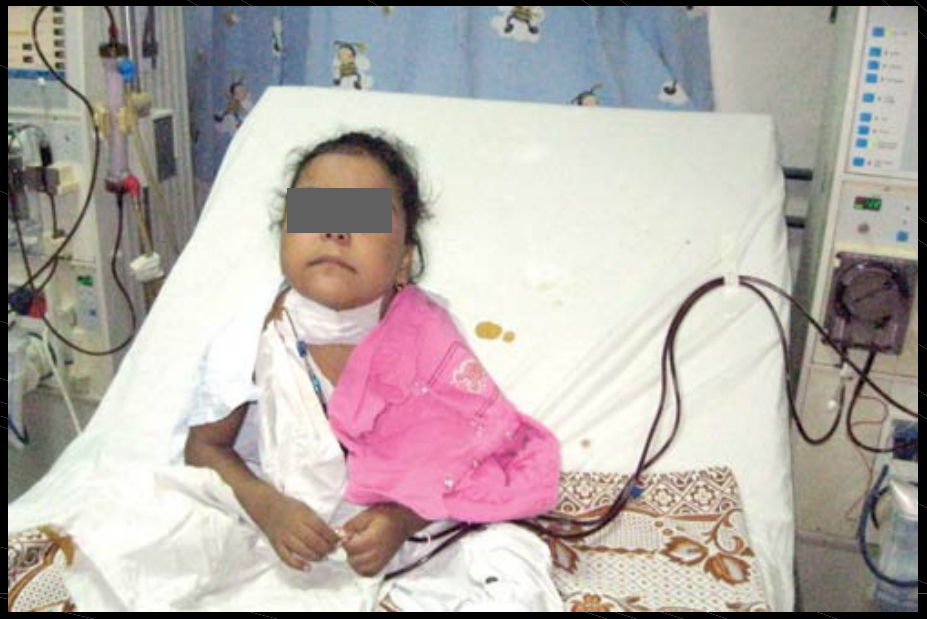
Each Stage was carried out in sequential sub-Stages of a particular Hemodialysis session designed to answer a particular research question.

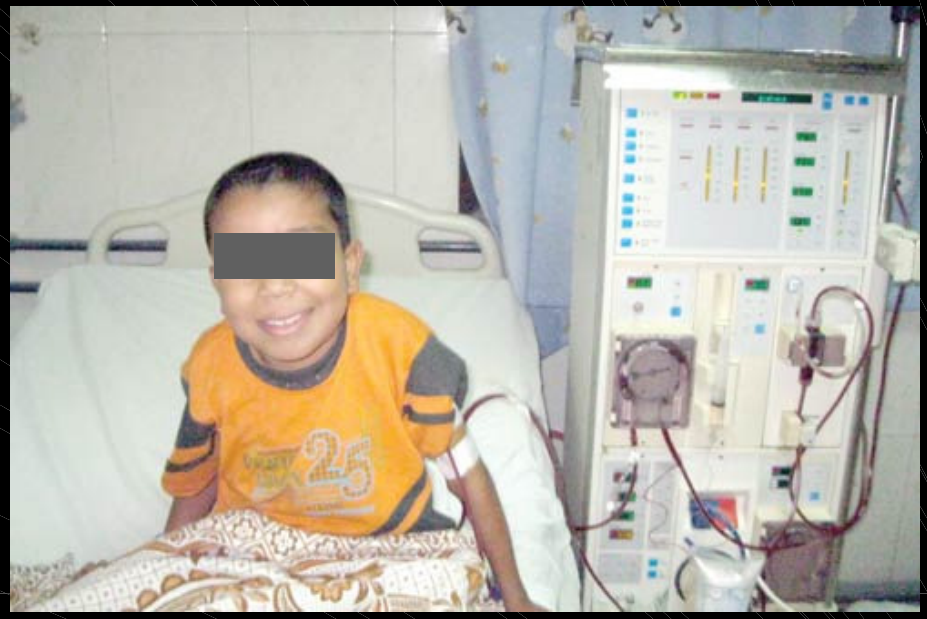
At the end of each Stage an interim analysis was done and recommendations for the coming Stage were given.

Methods - *Materials*

Connections were manufactured with a special order by Hydalina Medical© company, Egypt, from the same material as the traditional connections. The cost was around 2.7 $, per piece, compared to 1.8 per piece for the standard connections. Model AHD^{V} was assembled by adding 2 external valves at (R) and (P^{a}) to model AHD^{0}.

Methods - *Methods and Patient allocation*



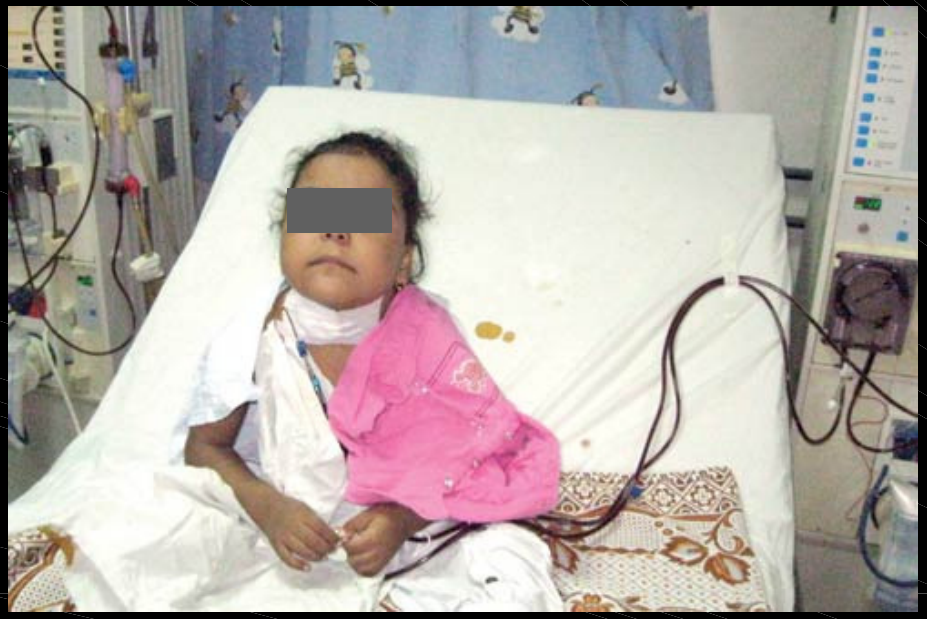


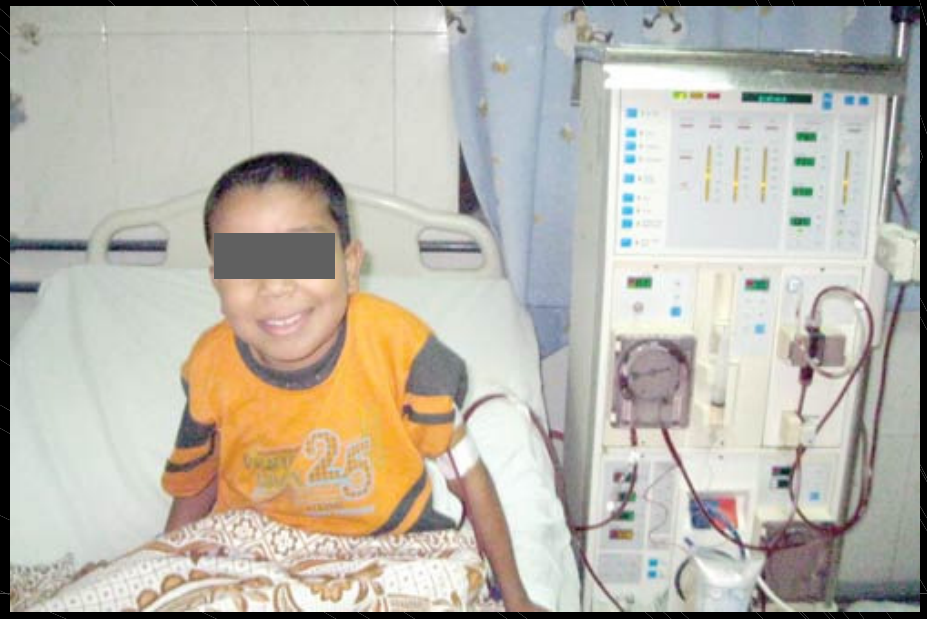
Criteria for Inclusion:

Children were included in the trial if:

- They had ESRD
- Were on routine hemodialysis for at least 3 months
- Had stable general condition
- No associated major cardiovascular or neurological illness
- They and their parents were willing to be included in the trial.

Methods - *Methods and Patient allocation*





Sampling

Ten children with ESRD were randomized to be enrolled in the trial using a random-number table. Children who fulfilled the selection criteria were allocated in 2 sequential Stages. Informed Verbal consent was obtained.

Methods - *Methods and Patient allocation*

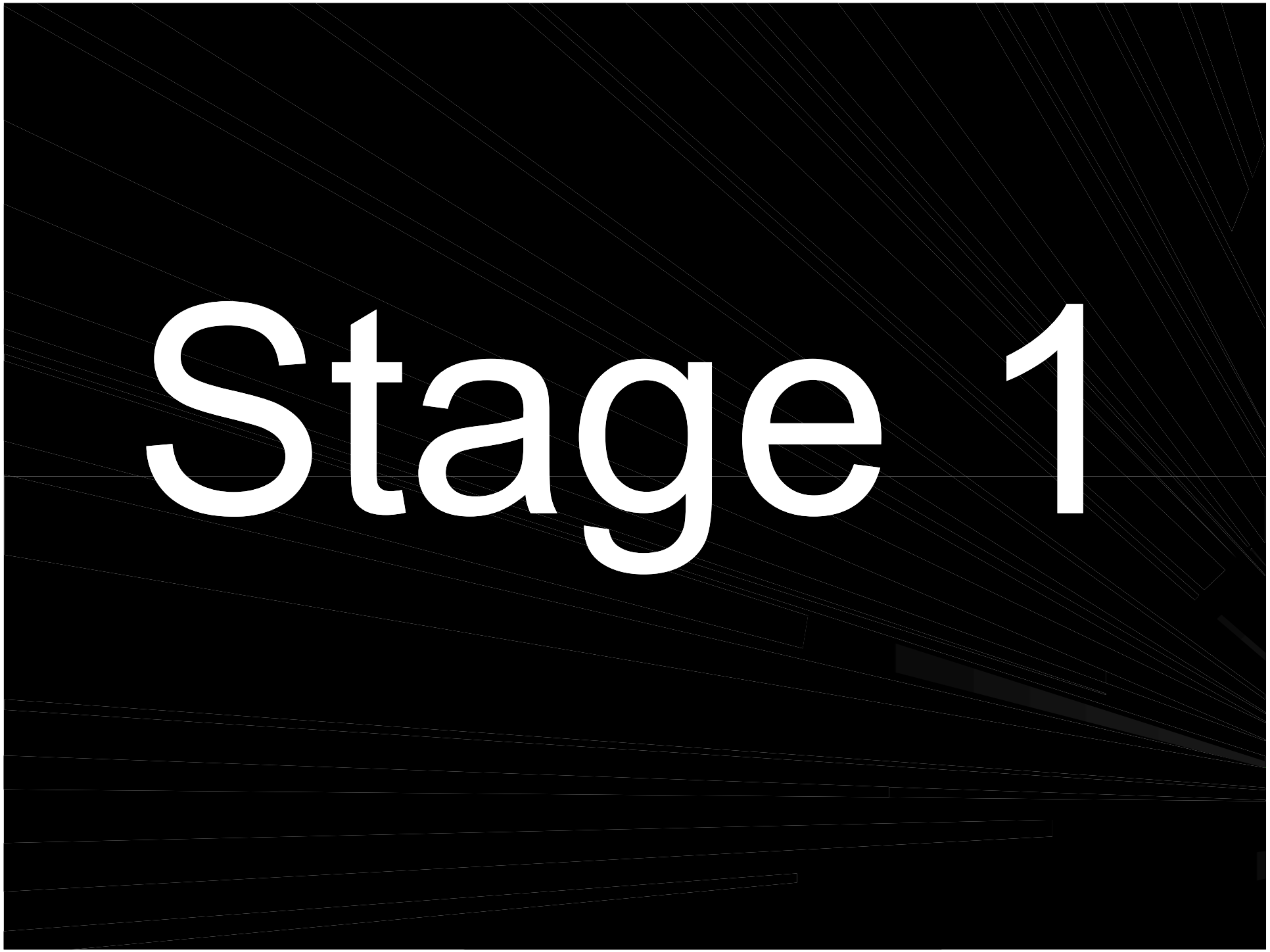
Out of around 50 children with ESRD on a chronic hemodialysis program, 10 children were enrolled in the study. The 10 children (6 boys and 4 girls) aged 8 - 16 years (mean= 10.93 years) with a dry body weight 15.5 - 26.6 kilogram (mean =22.14 kilogram). They were on the chronic hemodialysis program for 0.7 to 3.5 years (mean= 2.05 years). Dialysis was done using Freseinus hemodialysis filter. The session time was 3-3.5 hours (mean =3.2 hours).

Methods - *Methods and Patient allocation*

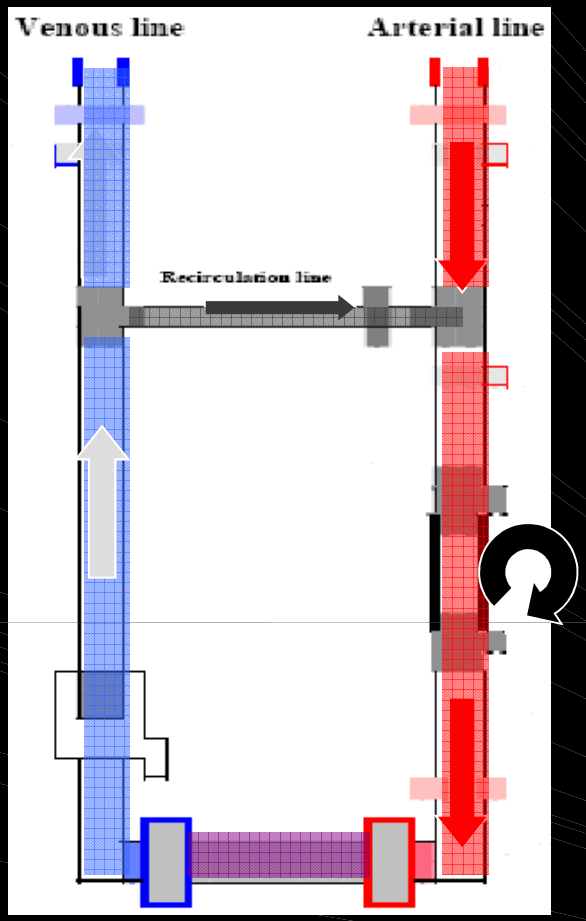
Routine heparin	Half heparin	No heparin R-AHD^{PR}
0.2 units/kg/minute	*0.1 units/kg/minute*	*Just flush*

In this article ;

- "Routine heparin" indicates a dose of 0.2 units/kg/minute.
- "Half heparin" indicates a dose of 0.1 units/kg/minute.
- "No heparin R-AHD^{PR}" indicates sessions without the use of heparin but the circuit was regularly flushed with normal saline.


Stage 1

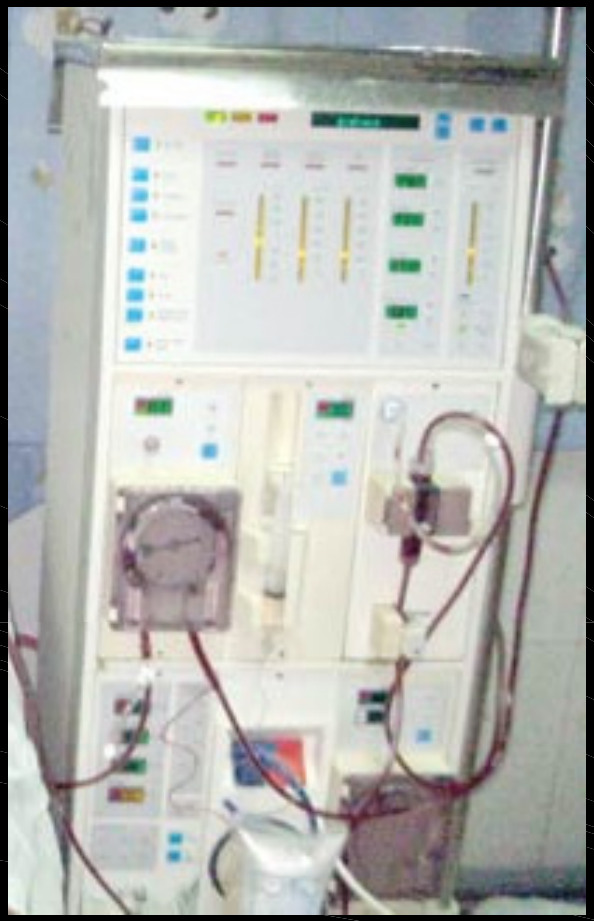
Methods - *Methods and Patient allocation*



R - AHD^0

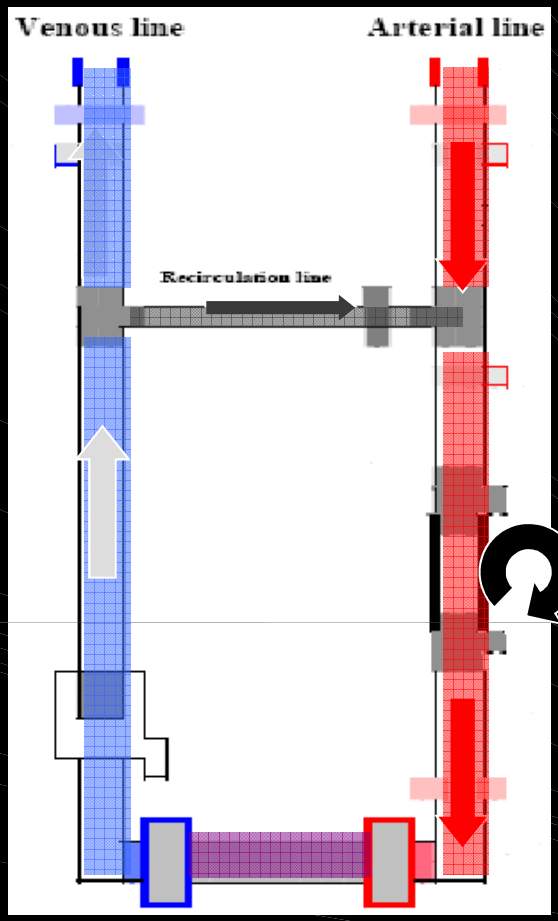
Stage 1 (R-AHD^0) was carried out using the AHD^0 connections

Methods - *Methods and Patient allocation*



AHD^0 connections were connected to a calibrated single blood pump Fresenius 4008B® hemodialysis machines.

Methods - *Methods and Patient allocation*



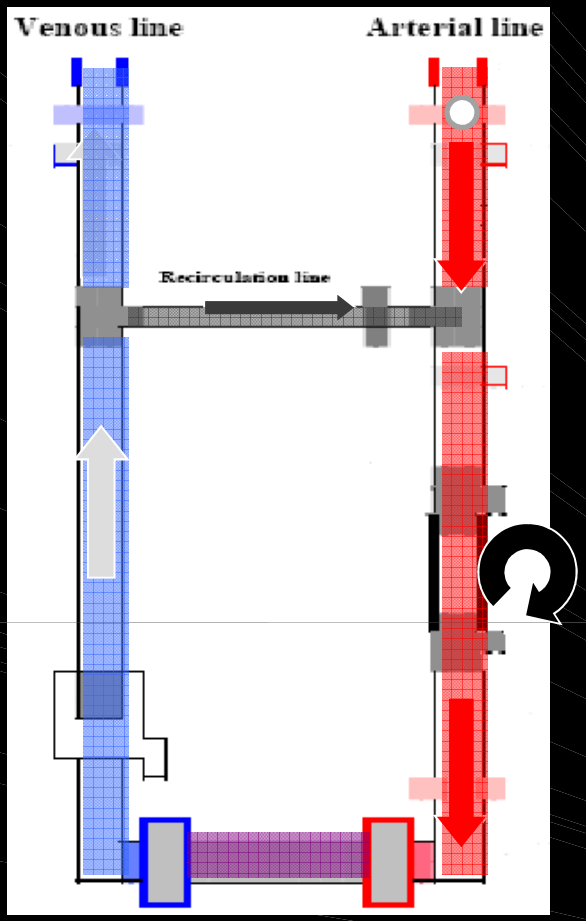
Target Patient BFR

Target Patient BFR X 3

R - AHD^0

The blood pump speed was initially adjusted to 3 folds the target patient BFR ,as the average patient/filter fluid flow rate of R-AHD^0 *in vitro* was 1:3

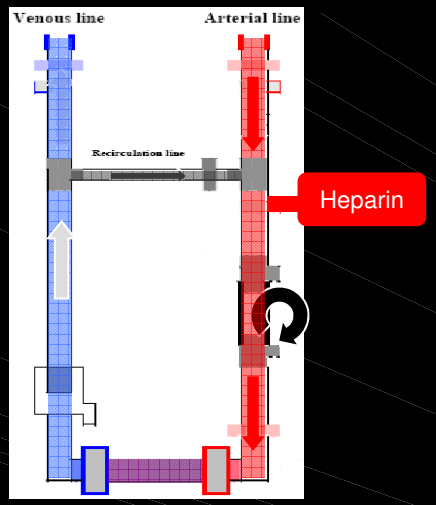
Methods - *Methods and Patient allocation*

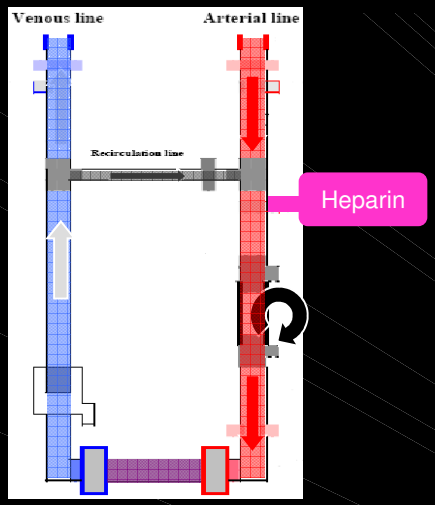


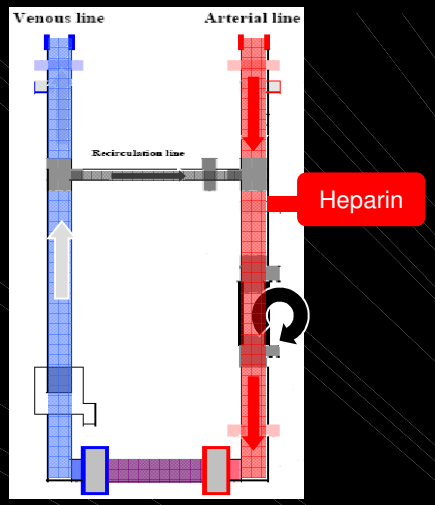
R - AHD^{0}

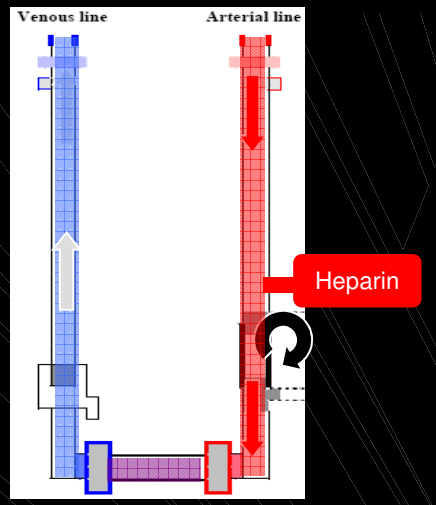
The blood pump speed was then readjusted guided by the speed of an air bubble through the patient portion of the arterial line as previously described by EL Hatw in 2006[11].

Methods – Stage 1





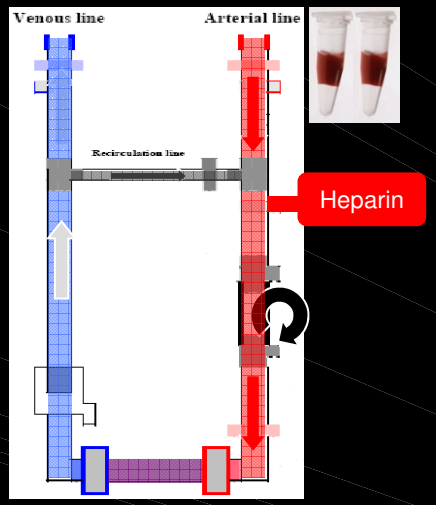


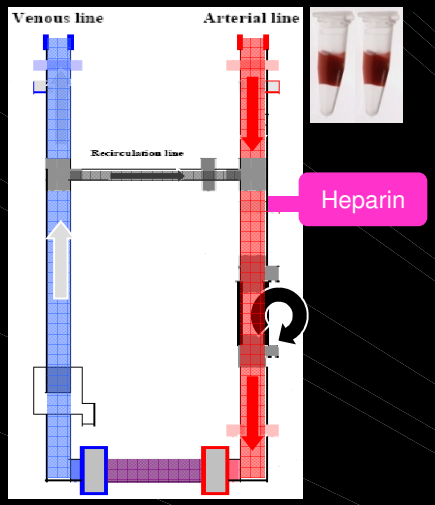


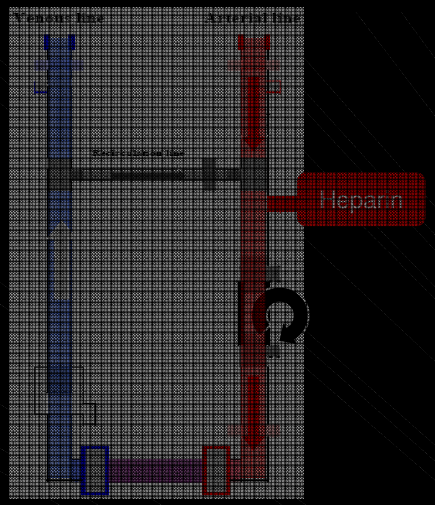
In **Stage 1**, the ten children passed 4 sequential sub-Stages

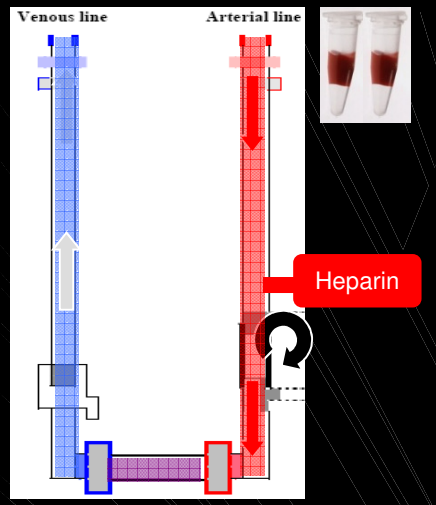
Stage 1a	Stage 1b	Stage 1c	Stage 1d
Routine heparin	Half heparin	Routine heparin	Routine heparin
R-AHD^0 sessions	R-AHD^0 sessions	R-AHD^0 sessions	DNHD sessions
10 children were treated with 10 sessions	10 children were treated with 10 sessions	One month of trice weekly sessions for 10 children (Total = 145 Sessions)	One month of trice weekly sessions for 10 children (Control)
Urea Reduction Ration (URR) of each session was measured	Urea Reduction Ration (URR) of each session was measured	At the end of the month URR, HB% and HT were measured.	At the end of the month URR, HB% and HT were measured.

Methods - Stage 1









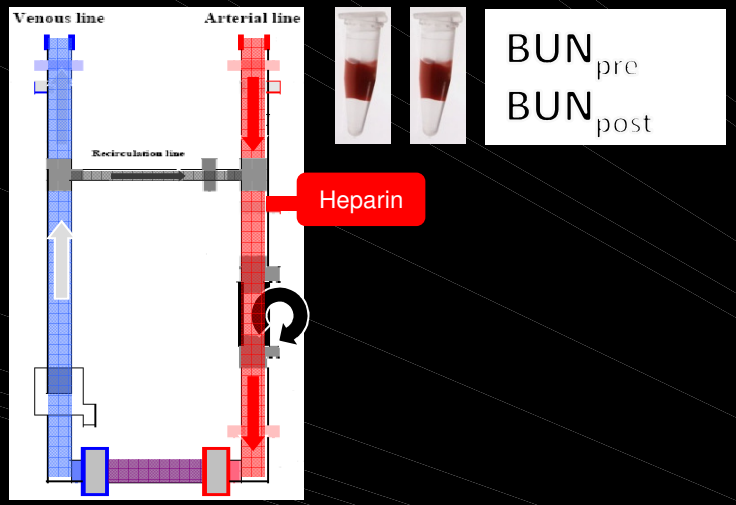
Stage 1a	Stage 1b	Stage 1c	Stage 1d
Routine heparin	Half heparin	Routine heparin	Routine heparin
R-AHD^0 sessions	R-AHD^0 sessions	R-AHD^0 sessions	DNHD sessions
10 children were treated with 10 sessions	10 children were treated with 10 sessions	10 children were treated with trice weekly for ≈ 1 Mo (Total = 145 Sessions)	10 children were treated with trice weekly for 1 Mo.

(A) Efficiency of the AHD; was studied by comparing the URR in

- R-AHD^0 (Stage 1a,b) and in
- DNHD sessions (Stage 1d) measured in the same patient.

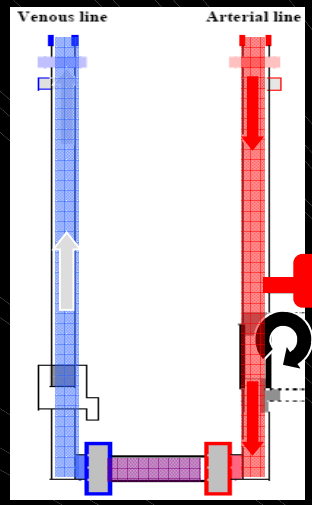
URR carries a possibility errors in calculating efficiency due to errors in post dialysis sampling or due to residual renal function

Methods - Stage 1



BUN_{pre}
BUN_{post}

R-AHD^0 session
Stage 1a,b



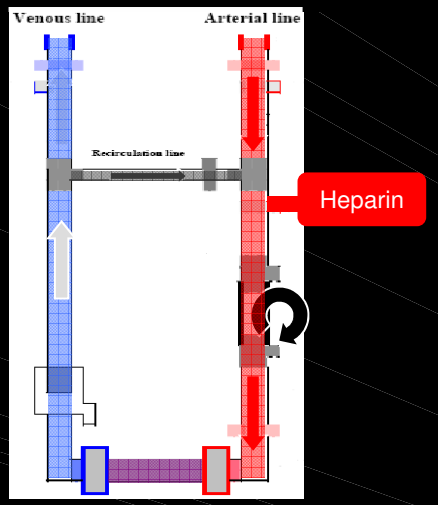
BUN_{pre}
BUN_{post}

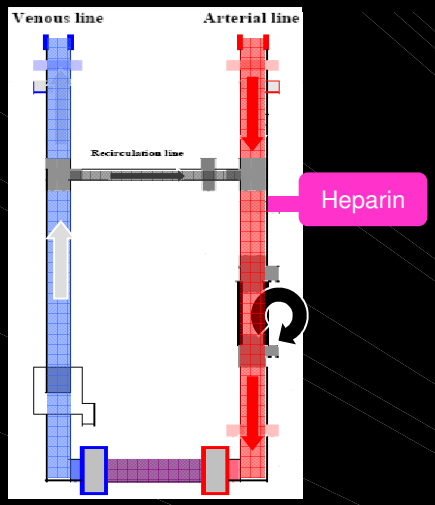
DNHD session
Stage 1d

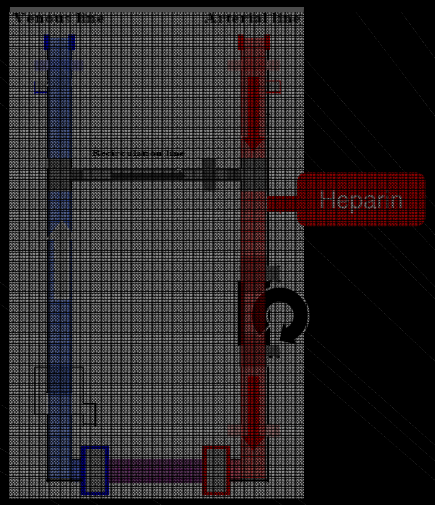
$$URR = BUN_{pre} - BUN_{post} / BUN_{pre} \times 100$$

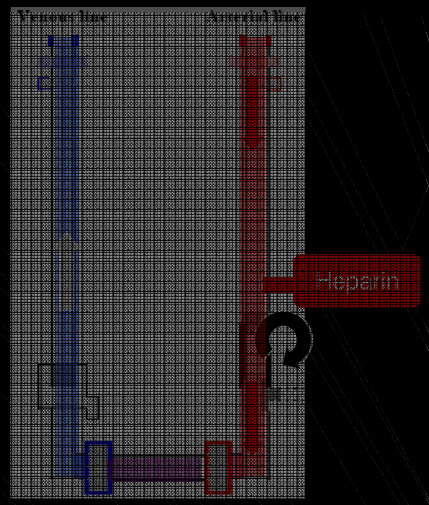
Urea reduction ratio of the tested session that was calculated as:
URR = Arterial BUN before the session – Arterial BUN after the session / Arterial BUN before the session X 100

Methods - Stage 1







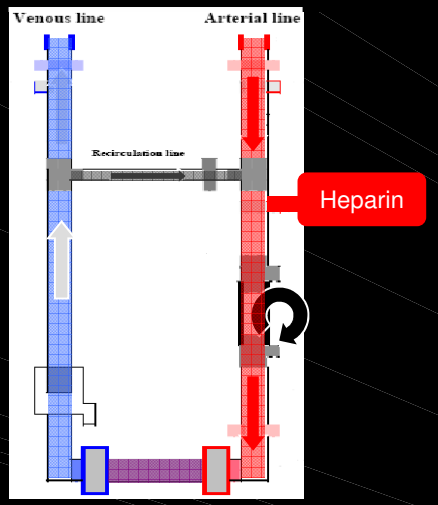


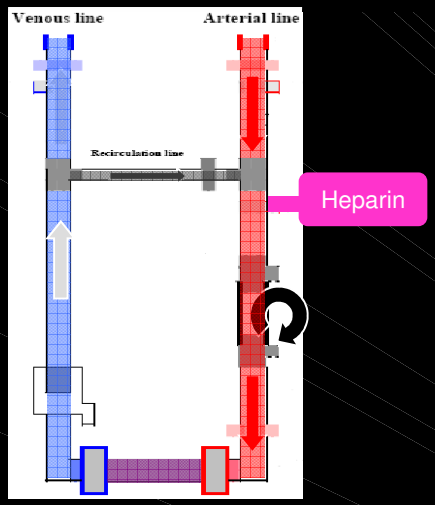
Stage 1a	Stage 1b	Stage 1c	Stage 1d
Routine heparin	Half heparin	Routine heparin	Routine heparin
R-AHD^0 sessions	R-AHD^0 sessions	R-AHD^0 sessions	DNHD sessions
10 children were treated with 10 sessions	10 children were treated with 10 sessions	10 children trice weekly for ≈ 1 Mo (Total = 145 Sessions)	10 children (Controls) trice weekly for 1 Mo.

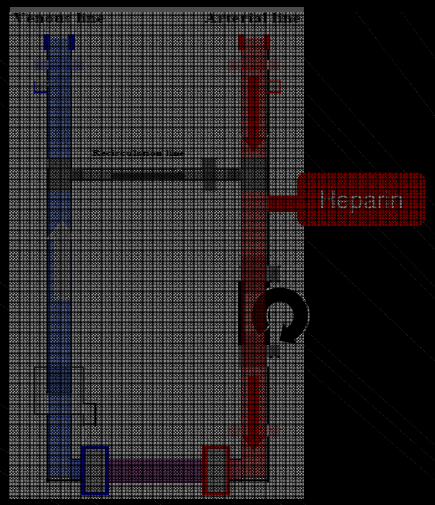
(B) The Anticoagulant effect of the AHD was studied by comparing incidence of blood clotting in :

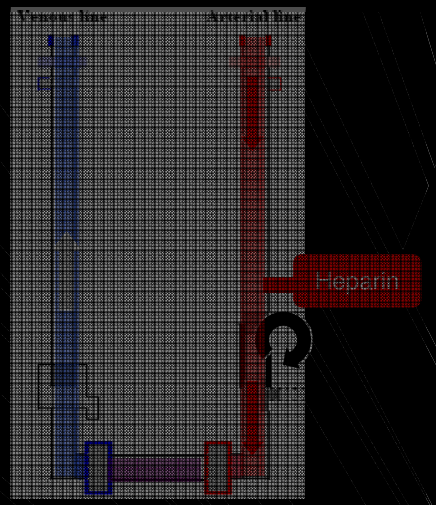
- The "Routine heparin R-AHD^0" **(Stage 1a)** and
- "½ dose heparin R-AHD^0" sessions **(Stage 1b)** .

Methods - Stage 1





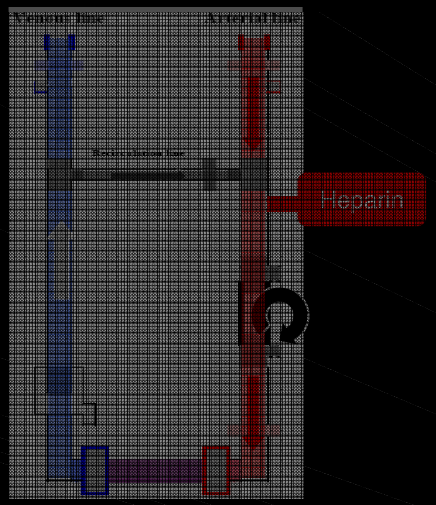


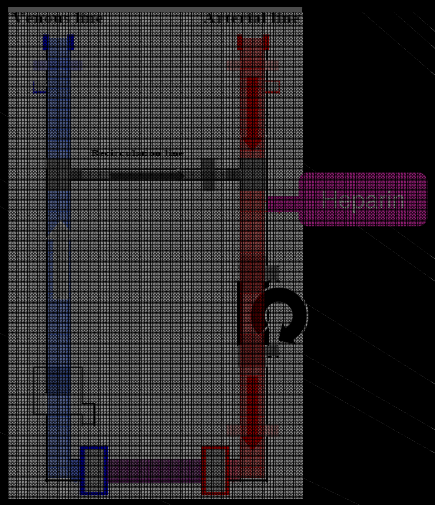


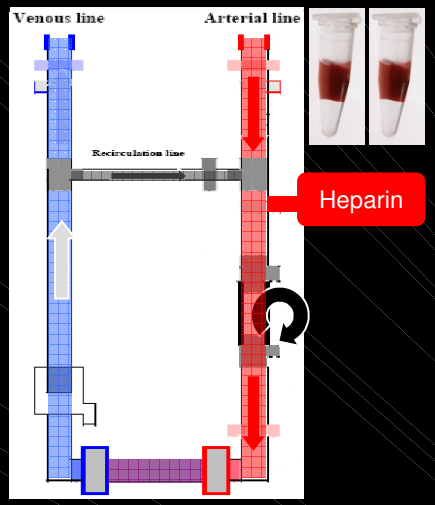
Stage 1a	Stage 1b	Stage 1c	Stage 1d
Routine heparin	Half heparin	Routine heparin	Routine heparin
R-AHD^0 sessions	R-AHD^0 sessions	R-AHD^0 sessions	DNHD sessions
10 children were treated with 10 sessions	10 children were treated with 10 sessions	10 children trice weekly for ≈ 1 Mo (Total = 145 Sessions)	10 children (Controls) trice weekly for 1 Mo.

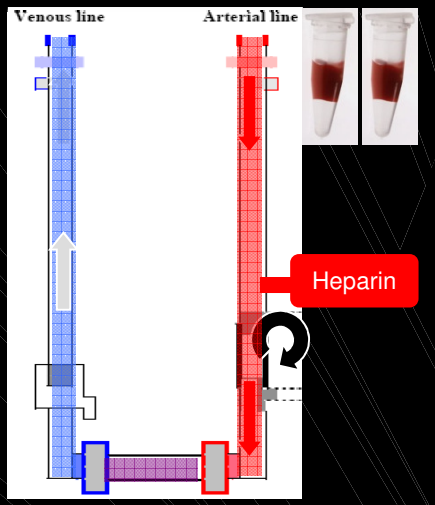
The long clotting time before starting the sessions indicates that the used "Routine dose heparin was actually a "high dose" of heparin with a prolonged residual anticoagulant effect.

Methods - Stage 1







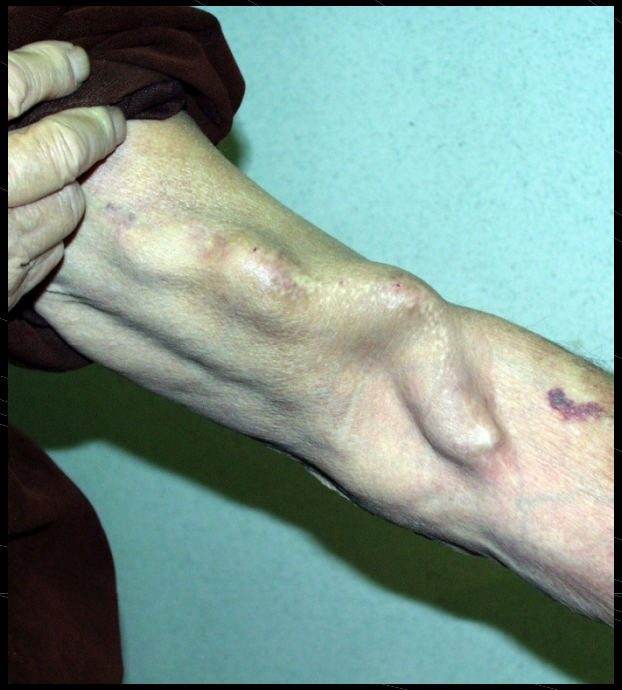


Stage 1a	Stage 1b	Stage 1c	Stage 1d
Routine heparin	Half heparin	Routine heparin	Routine heparin
R-AHD^{0} sessions	R-AHD^{0} sessions	R-AHD^{0} sessions	DNHD sessions
10 children were treated with 10 sessions	10 children were treated with 10 sessions	10 children trice weekly for ≈ 1 Mo (Total = 145 Sessions)	10 children (Controls) trice weekly for 1 Mo.

(C) The safety and efficiency of using R-AHD^{O} for chronic dialysis, (the clinical feasibility) was studied by comparing HB% and URR after:

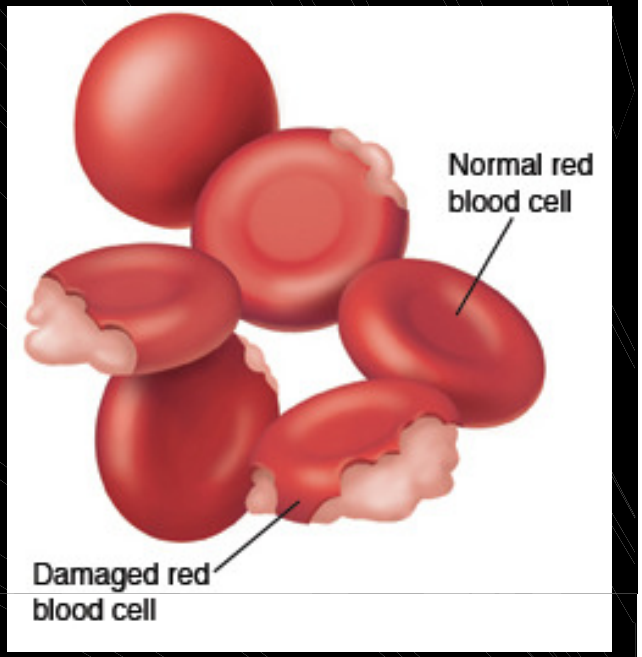
- One month of R-AHD^{O} (Stage 1c) &
- One month of DNHD (Stage 1d)

Methods - Stage 1



A-V fistula Integrity

Hollow fibers integrity

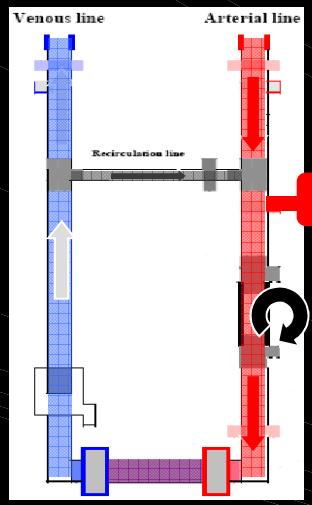


Drop of HB

The primary endpoint with respect to safety of using a high filter BFR were

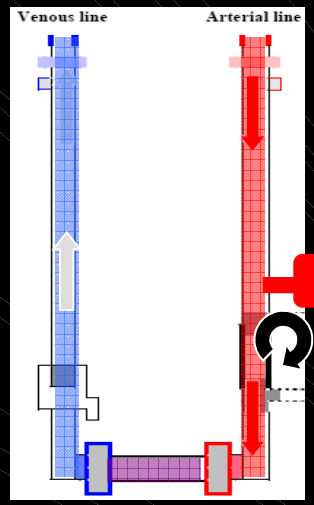
- Maintaining integrity of the A-V fistula
- Absence of blood leak alarms reflects integrity of the hollow fibers during the sessions
- Measuring the drop of HB after one month of trice weekly sessions.

Methods - Stage 1



URR
HB - HT

R-AHD^0 session
Stage 1c

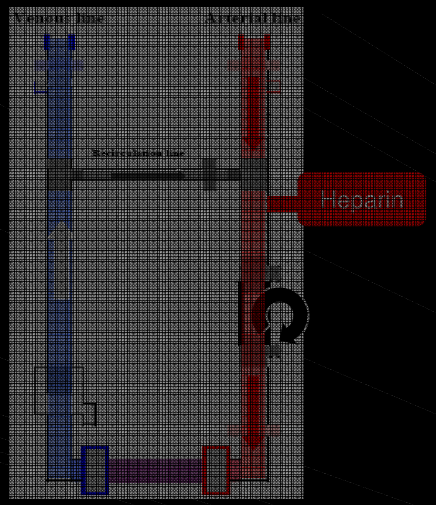


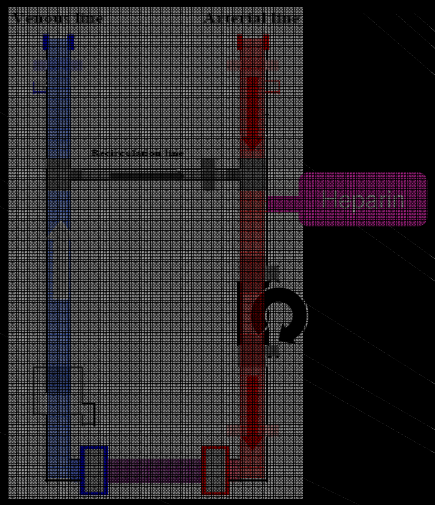
URR
HB - HT

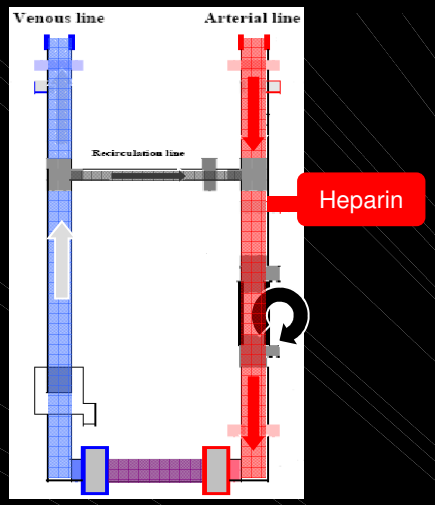
DNHD session
Stage 1d

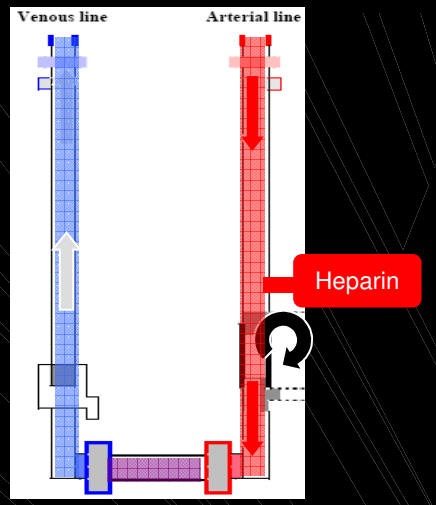
To assess the clinical feasibility of maintaining children with ESRD on routine R-AHD sessions, URR, HB% and HT were measured for each patient after one month of R-AHD^0 sessions and after one month of DNHD sessions.

Methods - In Stage 1, the ten children passed 4 sequential sub-Stages









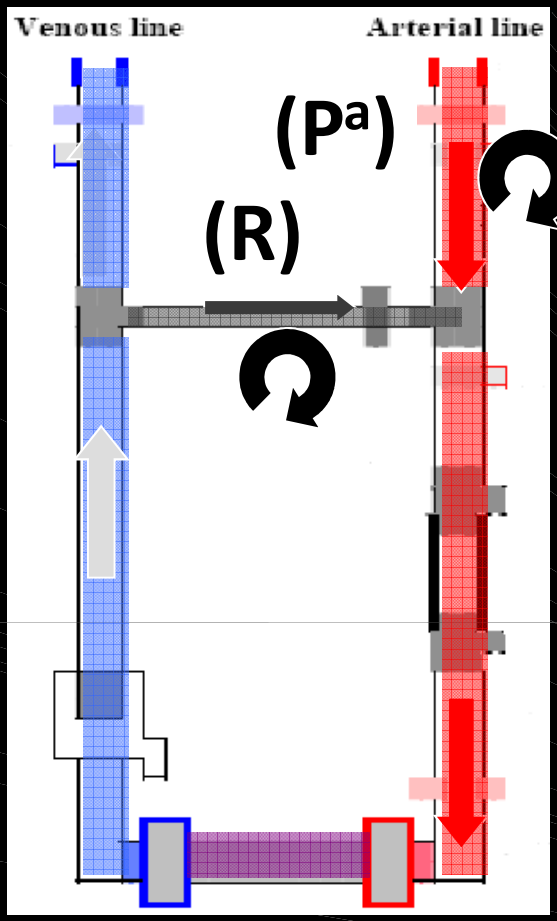
Stage 1a	Stage 1b	Stage 1c	Stage 1d
Routine heparin	Half heparin	Routine heparin	Routine heparin
R-AHD^{0} sessions	R-AHD^{0} sessions	R-AHD^{0} sessions	DNHD sessions
10 children were treated with 10 sessions	10 children were treated with 10 sessions	10 children trice weekly for ≈ 1 Mo (Total = 145 Sessions)	10 children (Controls) trice weekly for 1 Mo.

(C) Prove the efficiency and safety of using R-AHD^{O} for chronic hemodialysis by comparing the end of month URR and HB % after 1 month of:

- R-AHD^{O} **(Stage 1c)**
- DNHD **(Stage 1d)**


Stage 2

Methods - *Methods and Patient allocation*

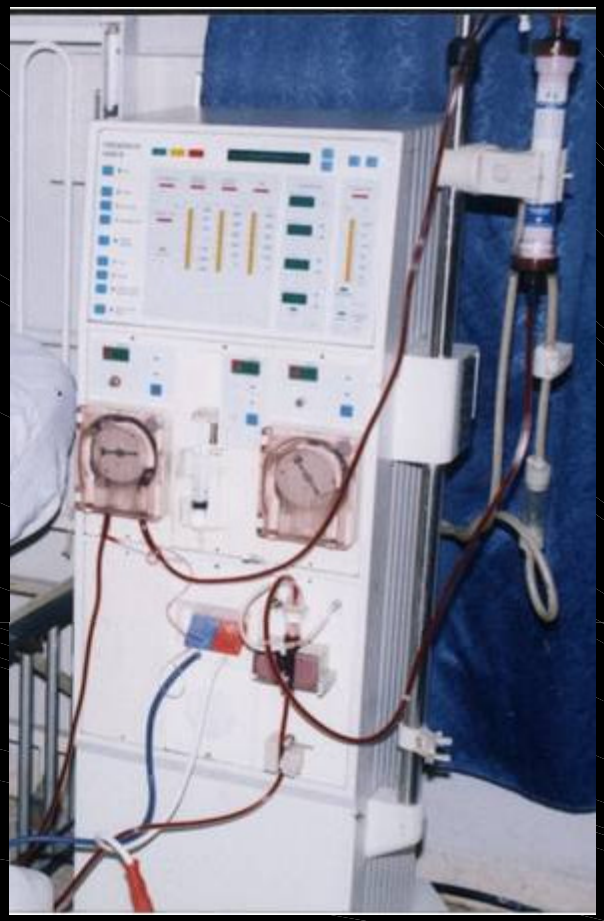


R - AHD^{PR}

Stage 2 was carried using the AHD^{PR} connections.

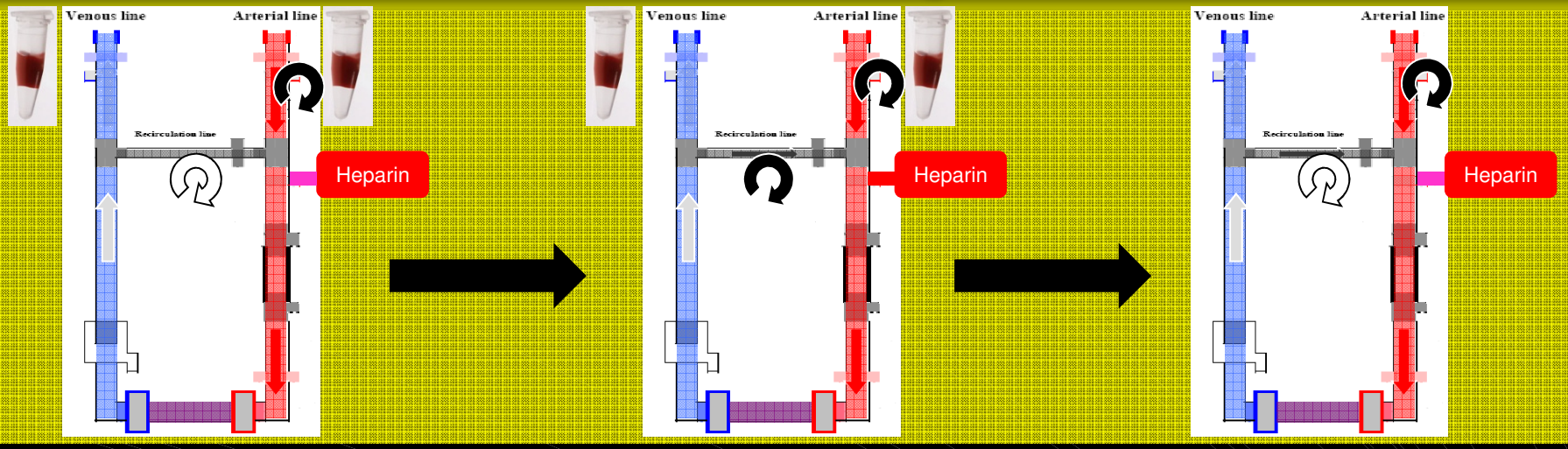
- The patient blood pump speed was adjusted to the target patient BFR.
- The recirculation blood pump speed was adjusted to achieve a
- Filter blood flow rate, equals the sum of patient and recirculation blood flow rate, of 500 ml/minute.

Methods - *Methods and Patient allocation*



AHD^{PR} connections were connected to a calibrated double blood pump Fresenius 2008B® hemodialysis machine. The software of this relatively old model allows direct operation and adjustment of the 2nd pump that is used as a recirculation pump.

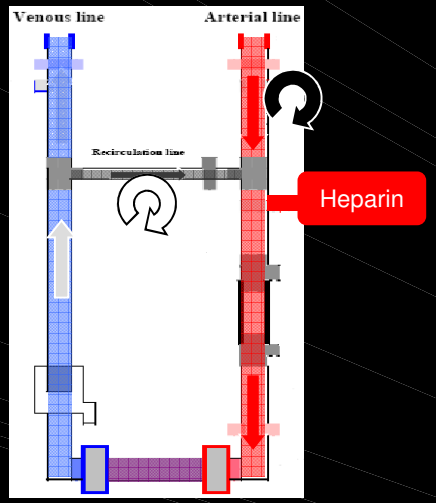
Methods - Stage 2

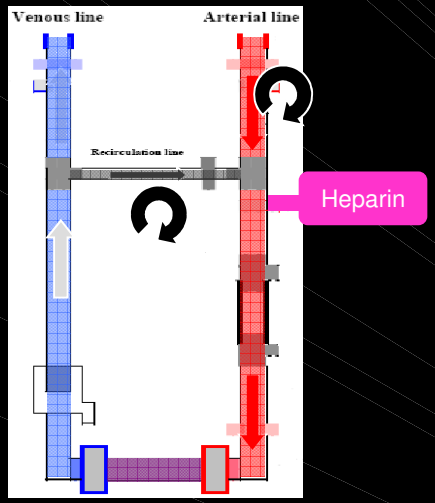


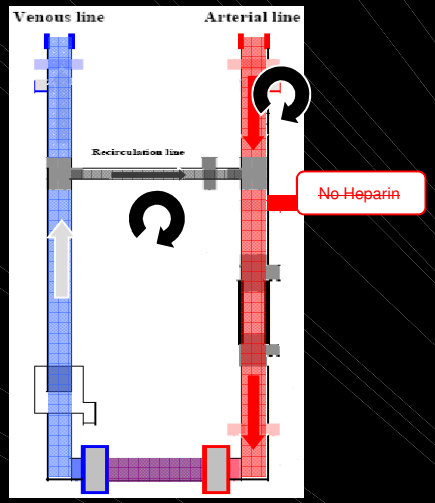
DNHD (15 min.) R – AHD^{FR} (15 min.) DNHD

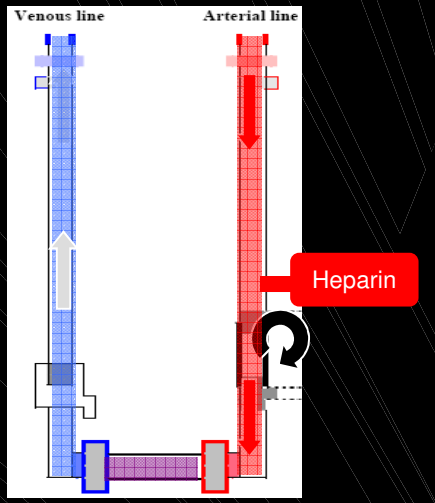
Stage 2a		
An initial 15 minutes of DNHD where the recirculation blood pump was switched off to close (R) and the patient BFR was adjusted to 5-10 ml/ kilogram/minute, then	15 minutes of R-AHD^{0} where the recirculation pump was switched on to achieve a sum filter BFR of 500 ml/minute	Then DNHD was restored till the end of the session.

Methods - Stage 2





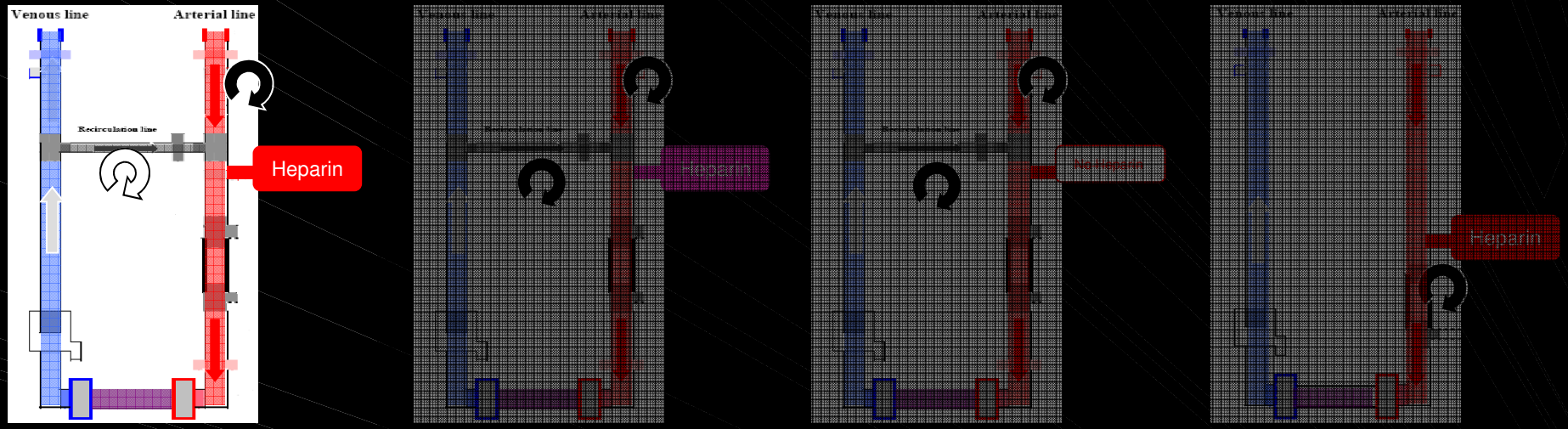




In **Stage 2**, the 10 children passed 4 sequential sub-Stages…

Stage 2a	Stage 2b	Stage 2c	Stage 2d
Routine heparin	Low heparin	No heparin	Routine heparin
mixed DNHD/AHD^{PR} sessions	*Low heparin R-AHD^{PR}*	*R-AHD^{PR}*	DNHD sessions
10 children were treated with 10 Sessions	8 children were treated with 8 Sessions.	One patient was treated with 10 subsequent sessions	10 children were treated with

Methods - Stage 2



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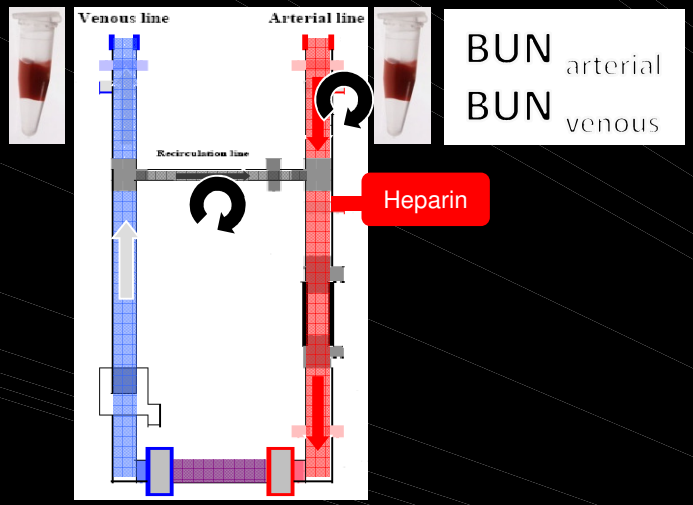
10 children were treated with 10 Sessions	8 children were treated with 8 Sessions.	One patient was treated with 10 subsequent sessions	10 children were treated with

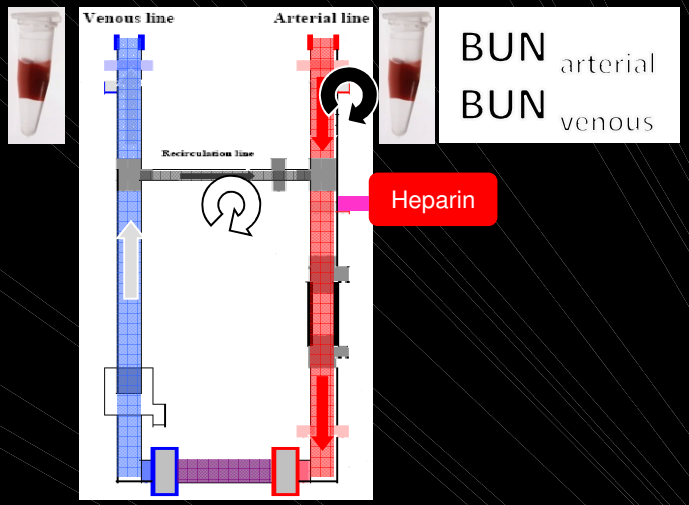
(A) Stage 2a was designed to study the Efficiency of the R-AHD^{PR}, by comparing

- F-URR in R-AHD^{PR} period with
- F-URR in DNHD period in the same session.

Methods - Stage 2



R-AHD^{PR} period
Stage 2a

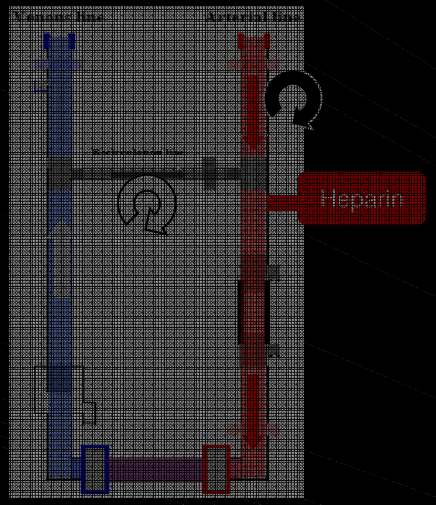


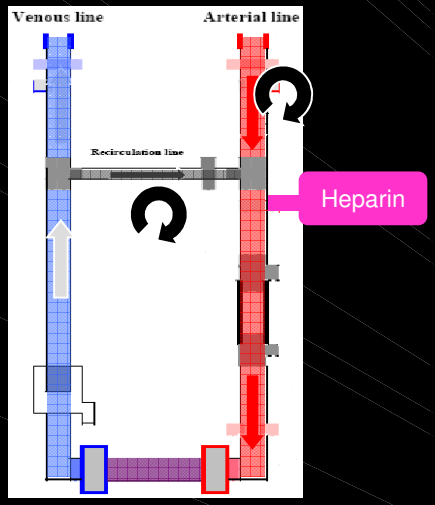
DNHD period
Stage 2a

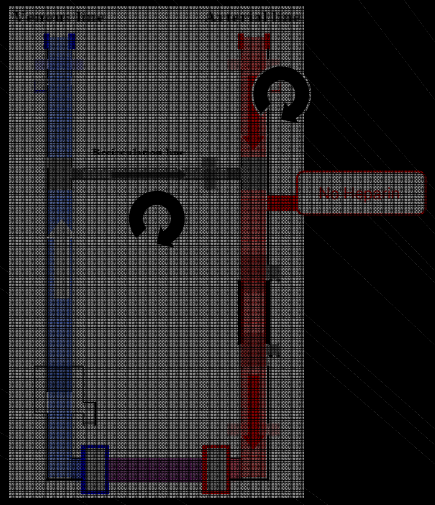
$$\text{F- URR} = \text{BUN}_{\text{arterial}} - \text{BUN}_{\text{venous}} / \text{BUN}_{\text{arterial}} \text{ X } 100$$

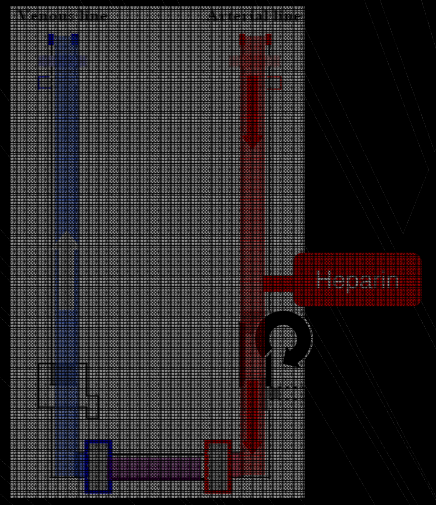
F-URR was is calculated as the difference between the arterial and venous BUN, divided by the arterial BUN, expressed in the percentage . Comparison of F-URR in the 2 periods of the same session overcomes errors due to post-dialysis blood sampling or due to the effect of the residual renal functions that may arise on comparing URR of 2 different sessions.

Methods - Stage 2





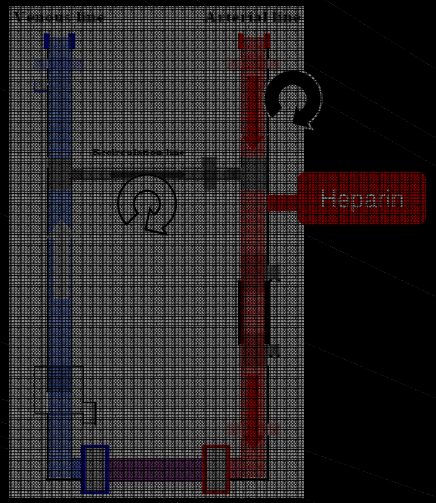


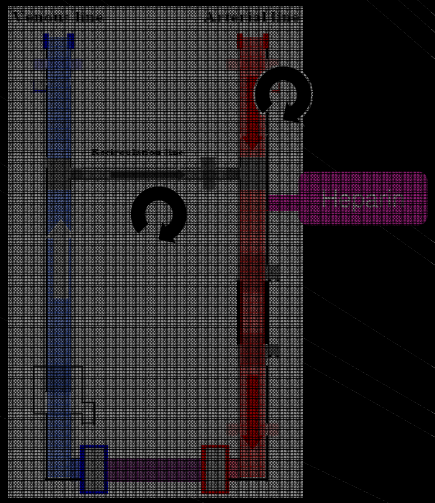


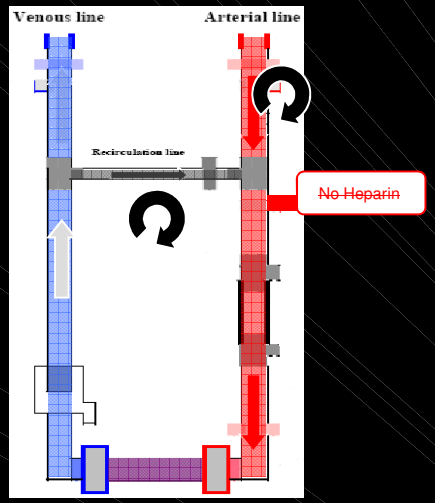
Stage 2a	Stage 2b	Stage 2c	Stage 2d
Routine heparin	Low heparin	No heparin	Routine heparin
mixed DNHD/AHD^{PR} sessions	*R-AHD^{PR}*	*R-AHD^{PR}*	DNHD sessions
10 children were treated with 10 Sessions	8 children were treated with 8 Sessions.	One patient was treated with 10 subsequent sessions	10 children were treated with

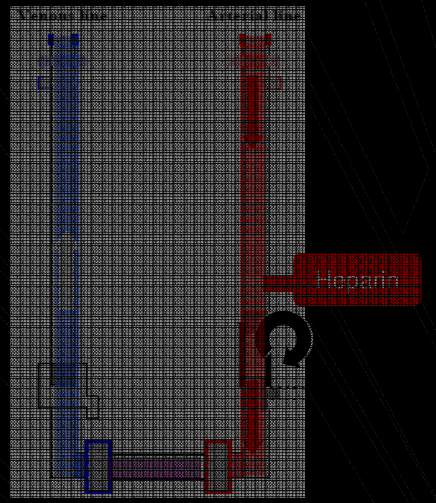
Connections were flushed with normal saline and the dose of the infused heparin throughout the session was adjusted to keep the prothrombin time (PTT) just above 140% of the initial values. Blood clotting data were collected in this session.

Methods - Stage 2





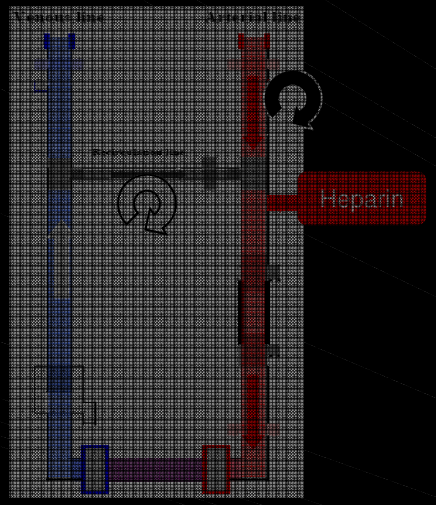


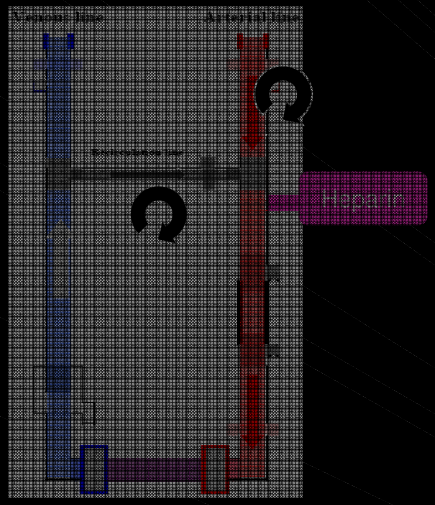


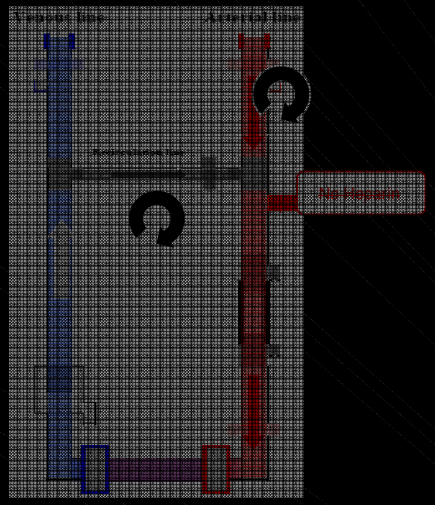
Stage 2a	Stage 2b	Stage 2c	Stage 2d
Routine heparin	Low heparin	No heparin	Routine heparin
mixed DNHD/AHD^{PR} sessions	*R-AHD^{PR}*	*R-AHD^{PR}*	DNHD sessions
10 children were treated with 10 Sessions	8 children were treated with 8 Sessions.	One patient was treated with 10 subsequent sessions	10 children were treated with

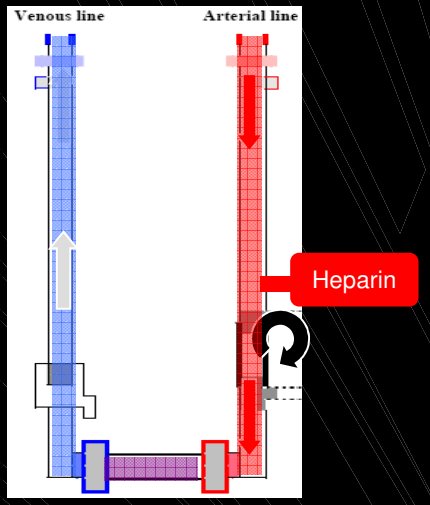
Connections were regularly flushed with normal saline, three times per week for a period of approximately 3 weeks. Blood clotting data were documented.

Methods - Stage 2





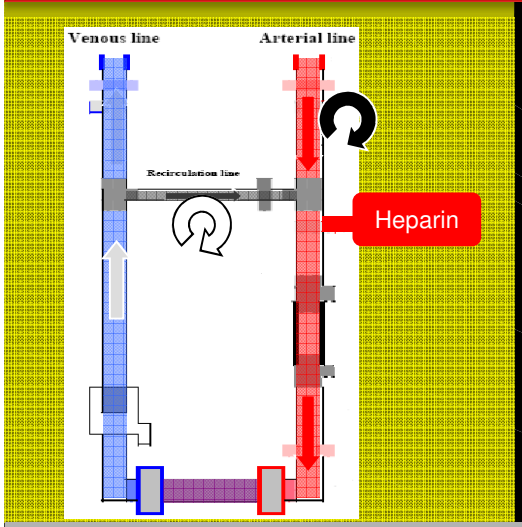


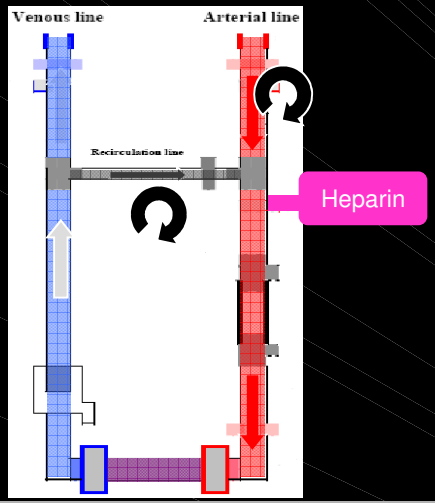


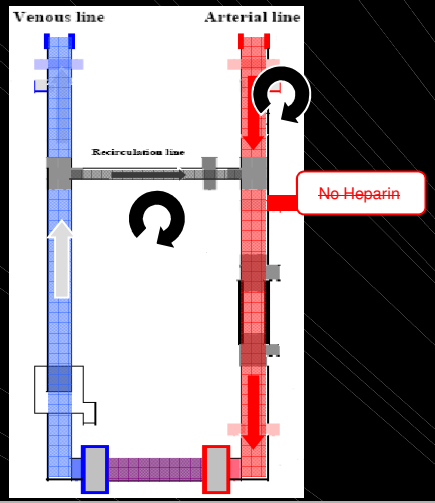
Stage 2a	Stage 2b	Stage 2c	Stage 2d
Routine heparin	Low heparin	No heparin	Routine heparin
mixed DNHD/AHD^{PR} sessions	*R-AHD^{PR}*	*R-AHD^{PR}*	DNHD sessions
10 children were treated with 10 Sessions	8 children were treated with 8 Sessions.	One patient was treated with 10 subsequent sessions	10 children were treated with trice weekly sessions

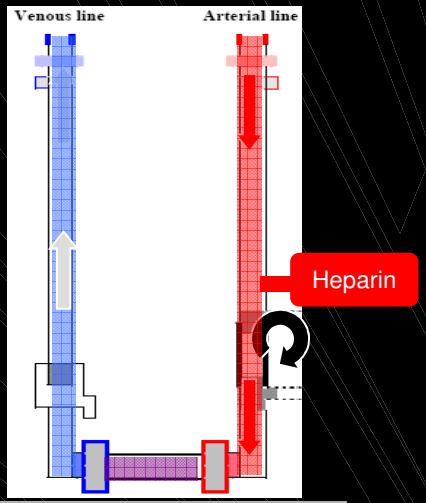
The total dose of heparin was measured. Arterial and venous samples were taken simultaneously to measure $BUN_{arterial}$ and BUN_{venous}

Methods - Stage 2





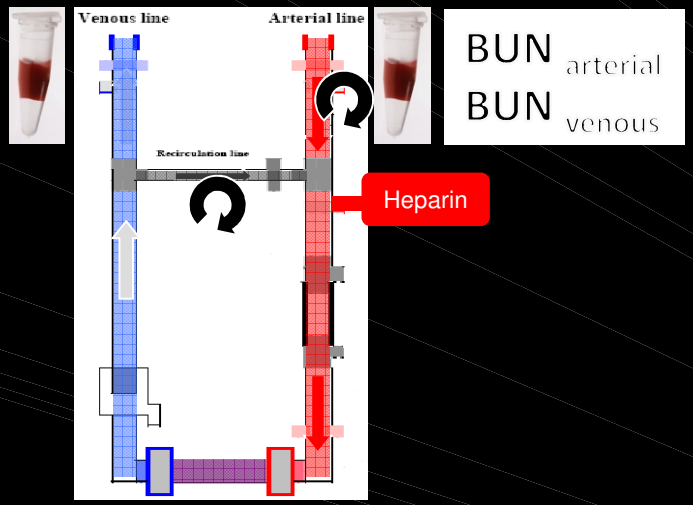




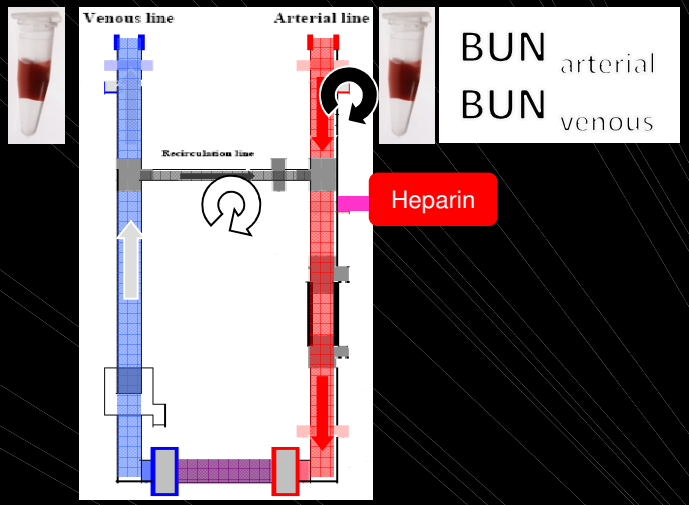
In *Stage 2*, the 10 children passed 4 sequential sub-Stages…

Stage 2a	Stage 2b	Stage 2c	Stage 2d
Routine heparin	Low heparin	No heparin	Routine heparin
mixed DNHD/AHD^{PR} sessions	*Low heparin R-AHD^{PR}*	*R-AHD^{PR}*	DNHD sessions
10 children were treated with 10 Sessions	8 children were treated with 8 Sessions.	One patient was treated with 10 subsequent sessions	10 children were treated with
efficiencies of AHD^{PR} and of DNHD periods were compared in the same session.	The patient blood pump speed was adjusted to the target patient BFR. The recirculation blood pump speed was adjusted to achieve a filter blood flow rate, equals the sum of patient and recirculation blood flow rate, of 500 ml/minute	where connections were also regularly flushed with normal saline, three times per week for a period of approximately 3 weeks. The details of the technique of the sessions are explained in (Appendix 1). Blood clotting data were documented	

Methods - *Data collection*



R-AHD^{PR} period
Stage 2a



DNHD period
Stage 2a

$$\text{F- URR} = \text{BUN}_{\text{arterial}} - \text{BUN}_{\text{venous}} / \text{BUN}_{\text{arterial}} \text{ X } 100$$

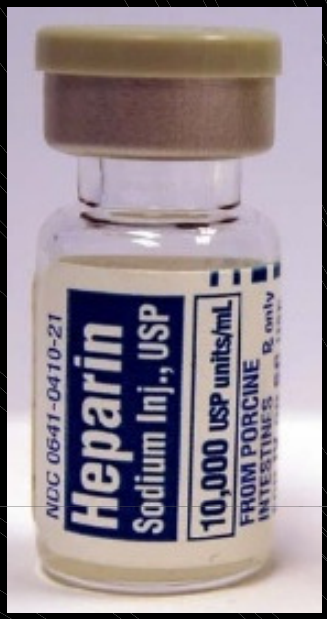
The primary endpoint with respect to efficacy of the R-AHD^{PR} and DNHD periods in the *"Routine heparin mixed (DNHD/AHD^{PR}) sessions"* was the ratio of reduction of BUN between the arterial and the venous ends measured after 15 minutes of each test period. In this article ,this ratio was referred to as The Filter Urea Reduction Ratio (F-URR) and was calculated as BUN in the arterial blood – BUN in the venous blood / BUN in arterial blood X 100

Methods - Stage 2

The primary endpoint of successful anticoagulation of a particular R-AHD sessions was the absence of evidence of blood clotting as

1. increased venous or arterial pressures
2. Darkening of blood in the filter and connections during the session or
3. Residual clots in the hollow fibers after the sessions.

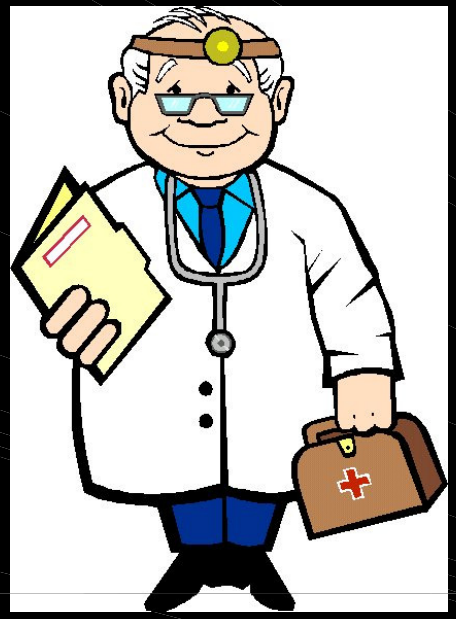
Methods - Stage 2

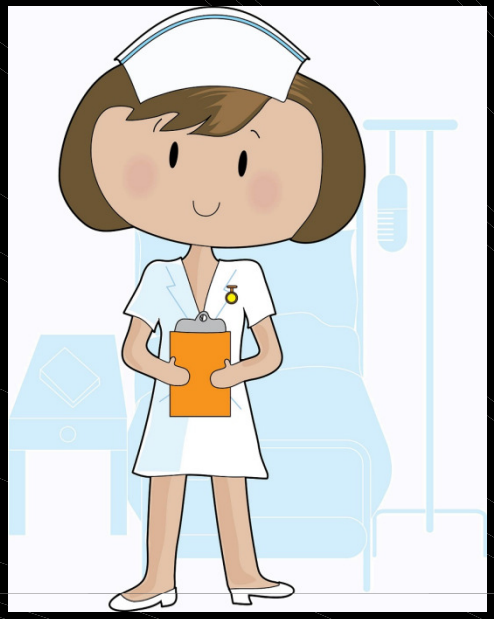


Additional relevant data were

1. The clotting time before the hemodialysis session to criticize the lasting effect of Routine heparin dose used in the previous dialysis session
2. The deviation of the achieved PTT values from the target value of 140% of the initial PTT to criticize the low heparin sessions as regards the accuracy in achieving the target PTT
3. The total dose of heparin per kg to criticize the low heparin sessions as regards to actual reducing of the heparin dose.

Methods - Data collection





Measure PTT in *Stage 2b*

Carrying out the hemodialysis sessions and collecting the blood samples were done by two assigned paid hemodialysis nurse in *Stage 1* and by a third nurse in *Stage 2* who was assisted by a laboratory technician to measure PTT in *Stage 2b*. All sessions were done under the supervision of one of the researchers and the patients received the routine monitoring and care as per the unit protocol.

Methods - Statistical methods

- **Descriptive statistics** were used to summarize the data. Frequencies (number of patients or number of sessions) and relative frequencies (percentages) were used when appropriate.

- **Matched t-test** was performed to compare continuous data . Composition of quantitative variables between the study groups in the present trial was carried out using Kruskal Wallis analysis of variance (ANOVA) test with multiple Mann Whiteny posthoc multiple 2- group comparisons.

- **Chi square ($\chi 2$) test** was performed to compare categorical data, .
- Yates correction was used instead when the expected frequency is less than 5.
- A probability value (ρ value) less than 0.05 was considered statistically significant.
- All statistical calculations were carried out using computer programs Microsoft Excel version 7 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc, Chicago IL, USA) statistical program.

Results

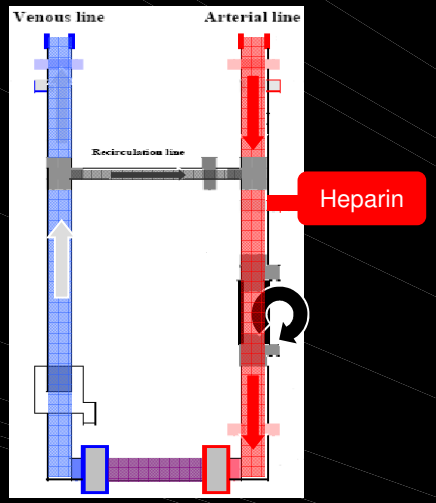
Results

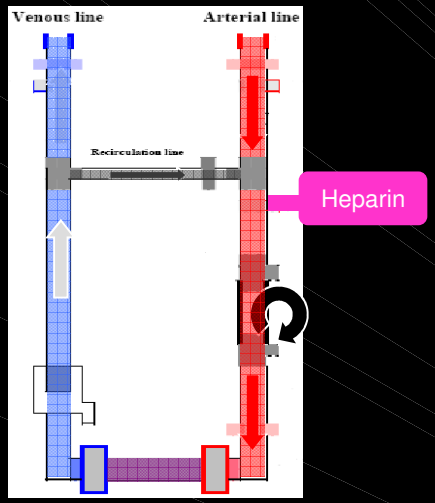
Blood clots appeared in 4 out of 165 R-AHD^{0} sessions but in none of the 28 R-AHD^{PR} sessions.

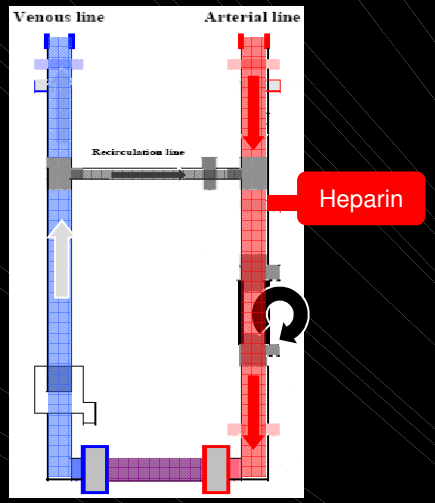
In *Stages 1;* mean URR was 0.597, 0.601 and 0.697 compared to 0.711 for the control (P>0.05).

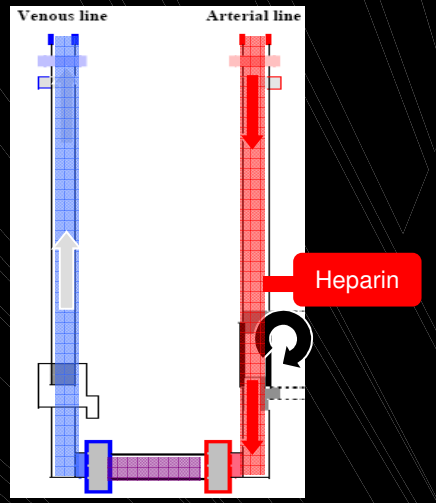
In *Stage 2,* the arterial BUN was reduced by 0.6592 ± 0.14555 after a R-AHD^{PR} period, compared 0.7869 ± 0.17722 after a DNHD period (P=0.059).

Results In R-AHD^0 sessions *(Stage 1)*







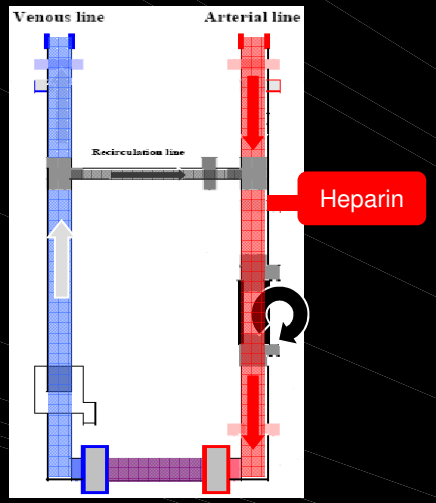


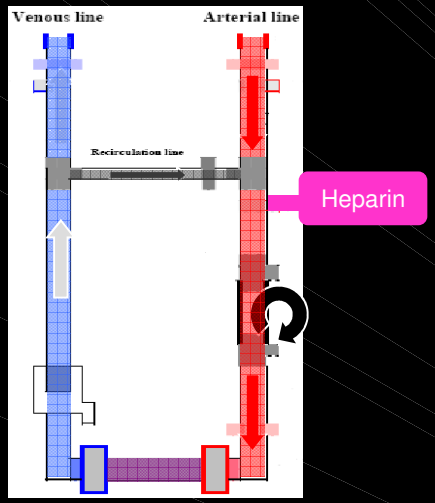
Stage 1a	Stage 1b	Stage 1c	Stage 1d
Routine heparin	Half heparin	Routine heparin	Routine heparin
R-AHD^0 sessions	R-AHD^0 sessions	R-AHD^0 sessions	DNHD sessions
Filter BFR = 400 - 450 ml/min. (mean = 444 ml/min.) Estimated patient BFR = 100 - 175 ml/ min. (mean 137.4 ml/min.)			BFR = 100 -150 ml/ min. (mean 124.5 ml/min.)

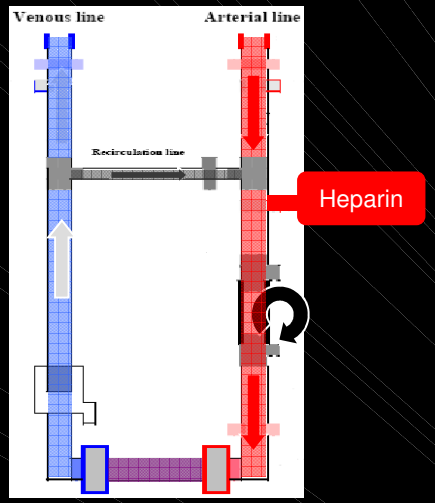
(P>0.05)

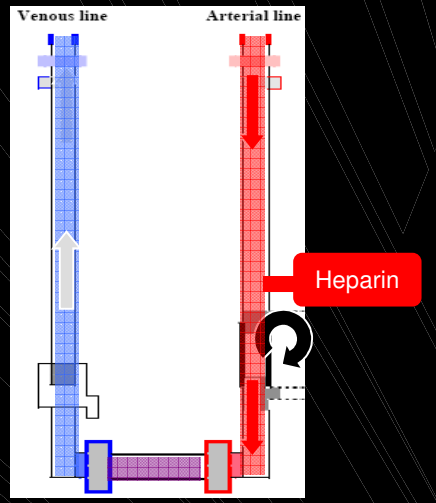
In **Stage 1,** there was no significant difference (P>0.05) between the patient blood flow rate between the accelerated sessions **(Stages 1a, 1b, 1c)** and the DNHD sessions **Stage 1d (control)**

Results In R-AHD^0 sessions *(Stage 1)*







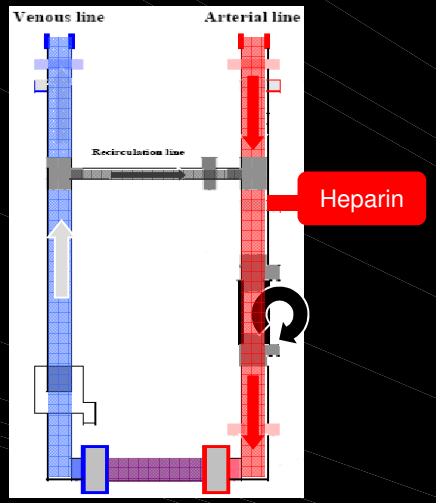


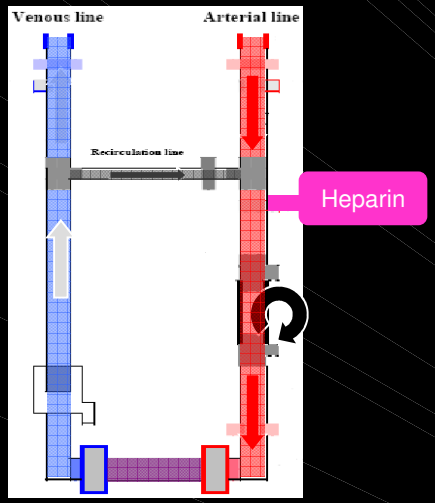
Stage 1a	Stage 1b	Stage 1c	Stage 1d
Routine heparin	Half heparin	Routine heparin	Routine heparin
R-AHD^0 sessions	R-AHD^0 sessions	R-AHD^0 sessions	DNHD sessions
The venous pressure: **Range: 82.5-143 mm Hg** **Mean: 125.4 mm Hg**			**The venous pressure:** **Range: 60-240 mm Hg** **Mean: 117.4 mm Hg**

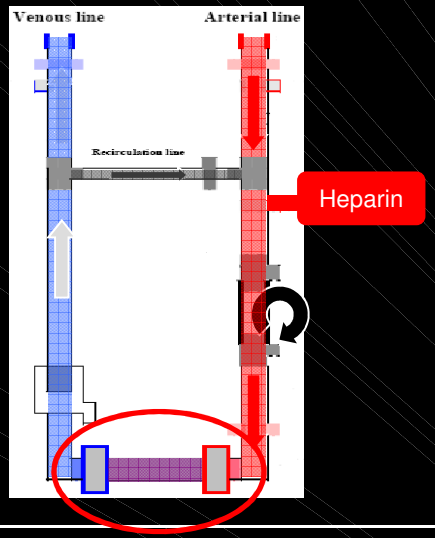
(P>0.05)

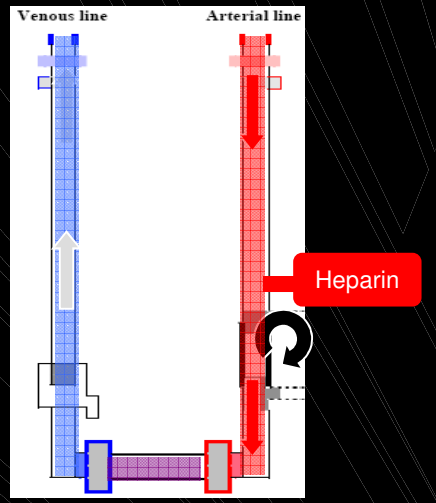
In **Stage 1,** there was no significant difference between the venous pressure between the accelerated sessions **(Stages 1a, 1b, 1c)** and the DNHD sessions **(Stage 1d)** in **Stage 1**

Results In R-AHD^0 sessions *(Stage 1)*



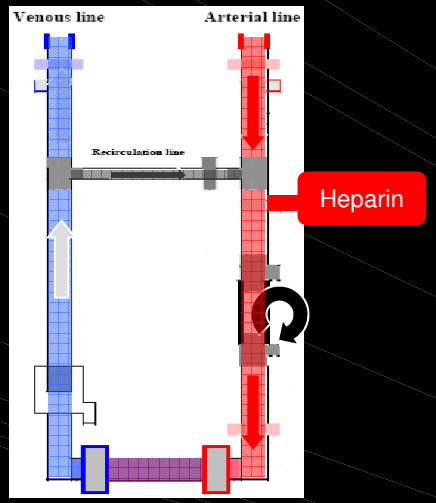


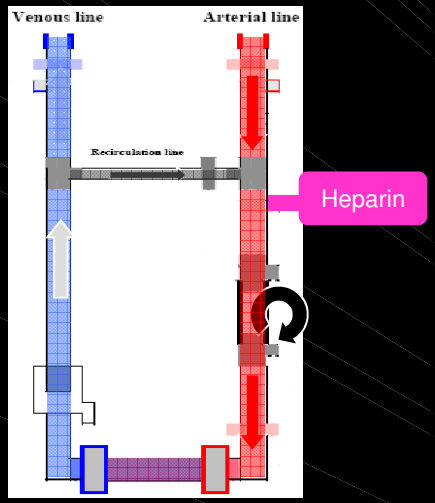


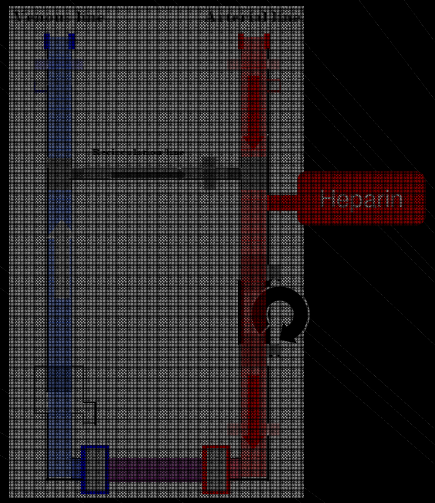


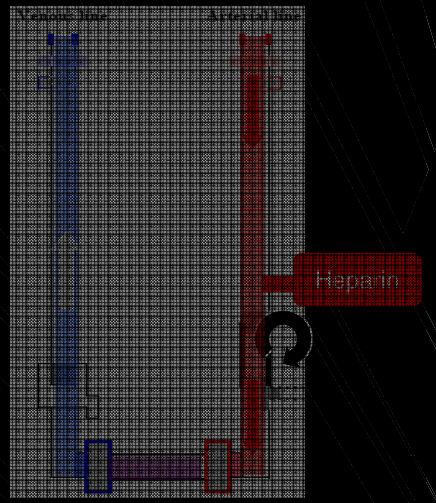
Stage 1a	Stage 1b	Stage 1c	Stage 1d
Routine heparin	Half heparin	Routine heparin	Routine heparin
R-AHD^0 sessions	R-AHD^0 sessions	R-AHD^0 sessions	DNHD sessions
No Blood Clotting	No Blood Clotting	blood clotting appeared in 4 out of 145 *sessions"* (2.76%) sessions: • Minor blood clots were detected at the venous blood fistula needle at the end of 3 sessions •A major clotting in the filter was detected near the end of the 4th session after which this Stage was terminated.	No Blood Clotting

Results In R-AHD^0 sessions *(Stage 1)*





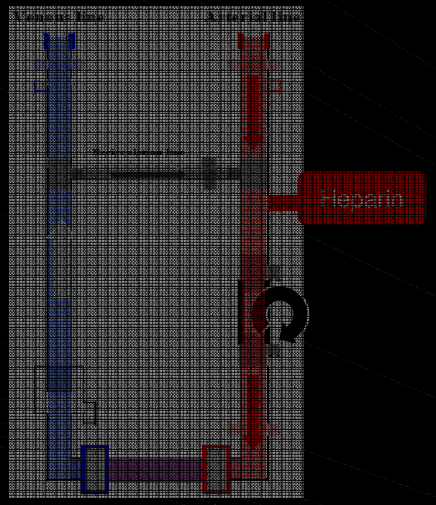


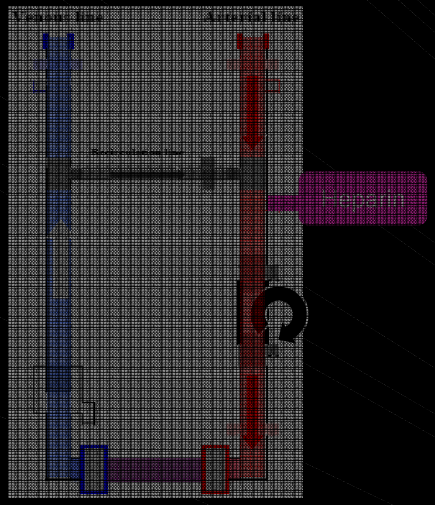


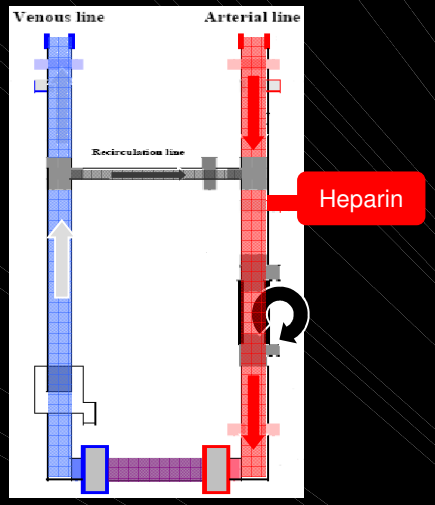
Stage 1a	Stage 1b	Stage 1c	Stage 1d
Routine heparin	Half heparin	Routine heparin	Routine heparin
R-AHD^0 sessions	R-AHD^0 sessions	R-AHD^0 sessions	DNHD sessions
Clotting time = 300 - 789 sec. (mean= 481 sec.) before the session	Clotting time = 300 - 1543 sec. (mean = 933 sec.) before the sessions		

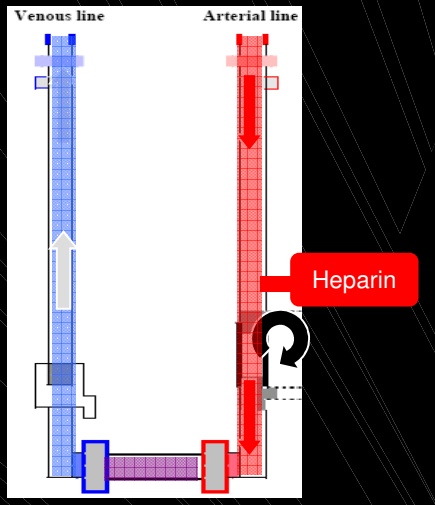
Clotting time was very high before the sessions in **Stage 1a** and in **Stage 1b** that reflects a high dose of heparin used in the previous session.

Results In R-AHD^0 sessions *(Stage 1)*







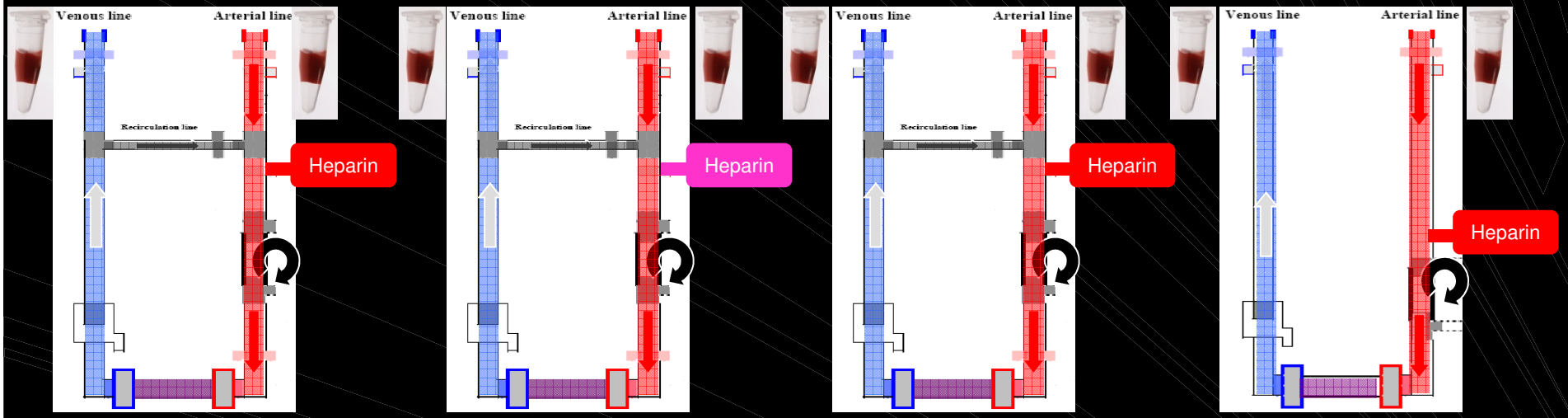


Stage 1a	Stage 1b	Stage 1c	Stage 1d
Routine heparin	Half heparin	Routine heparin	Routine heparin
R-AHD^0 sessions	R-AHD^0 sessions	R-AHD^0 sessions	DNHD sessions
		HB% (8-12.4) gm% mean 9.8 gm% HT (22.2- 35.4)gm% (mean=28) gm%	**HB% (8.6 - 12.6) gm% mean 10.3 gm% HT (24.4- 37.7) gm% mean= 30.5 gm%**

(P>0.05)

There was no significant difference between the HB and the HT after 1 month of accelerated sessions **(Stage 1c)** and the DNHD sessions **(Stage 1d)**.

Results In R-AHD^0 sessions *(Stage 1)*

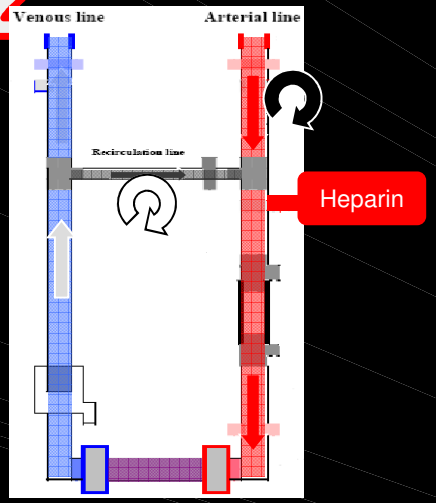


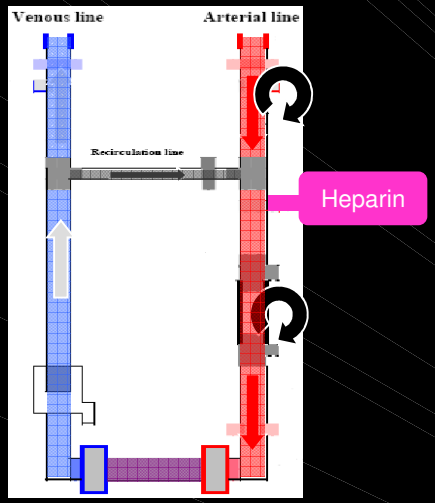
Stage 1a	Stage 1b	Stage 1c	Stage 1d
Routine heparin	Half heparin	Routine heparin	Routine heparin
R-AHD^0 sessions	R-AHD^0 sessions	R-AHD^0 sessions	DNHD sessions
Mean URR = 0.597	**Mean URR = 0.601**	**Mean URR = 0.697**	**Mean URR = 0.711**

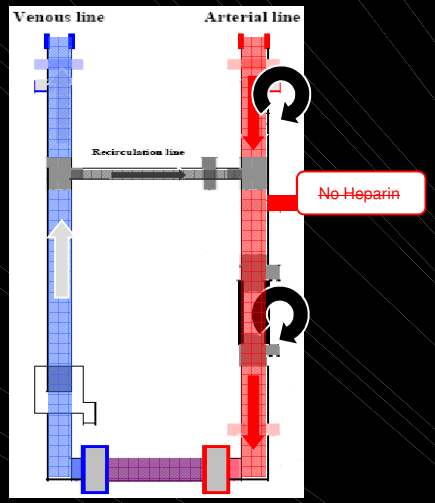
(P>0.05)

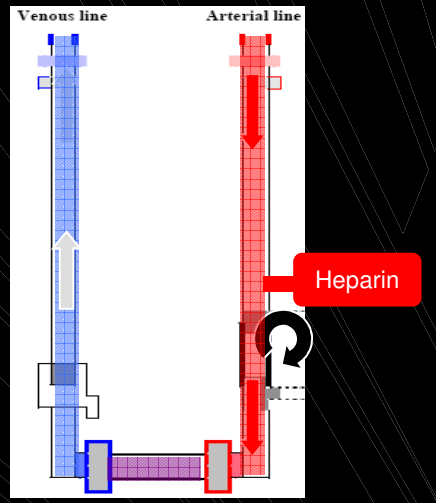
There was no significant difference between the mean URR in the AHD sessions **(Stage 1a**, **1b** and **1c)** compared to the DNHD session **(Stage 1d)** *(control)*.

2 Results In R-AHD^{PR} sessions *(Stage 2)*





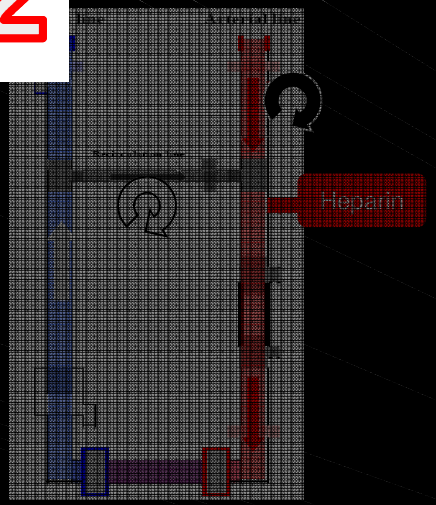


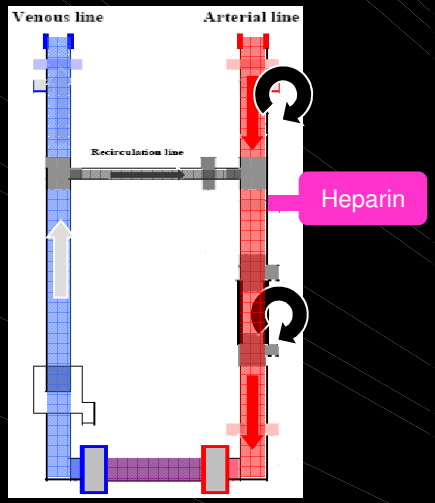


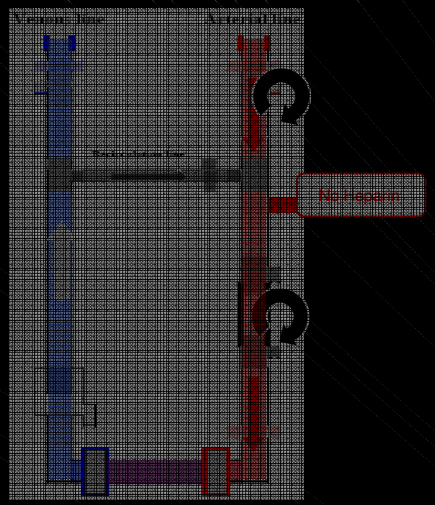
Stage 2a	Stage 2b	Stage 2c	Stage 2d
Routine heparin	Low heparin	No heparin	Routine heparin
mixed DNHD/AHD^{PR} sessions	*R-AHD^{PR}*	*R-AHD^{PR}*	DNHD sessions
No Blood Clotting	No Blood Clotting	No Blood Clotting	No Blood Clotting

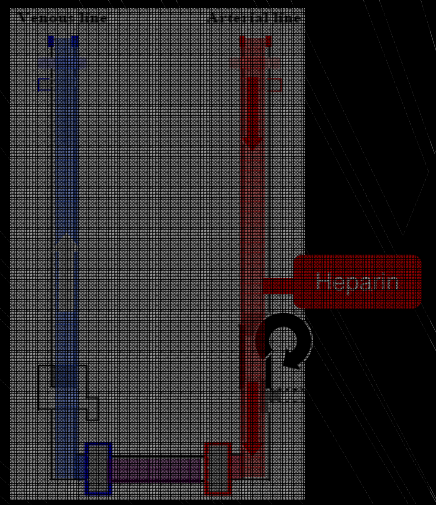
Blood clotting did not appear in **Stages 2a, 2b or 2c.**

2 Results In R-AHD^{PR} sessions *(Stage 2)*

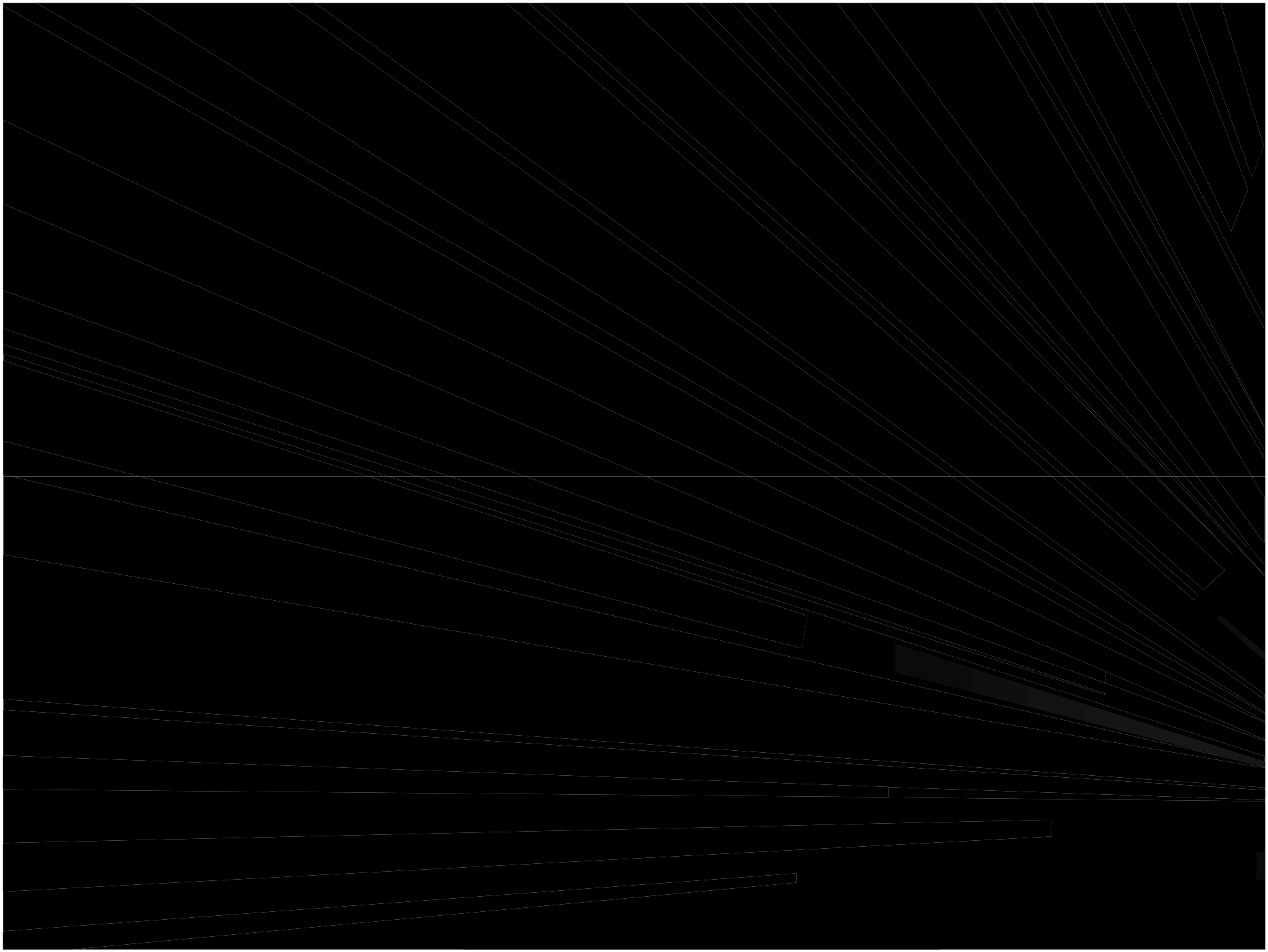




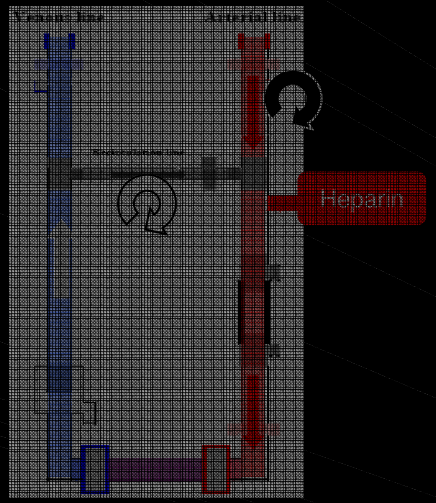


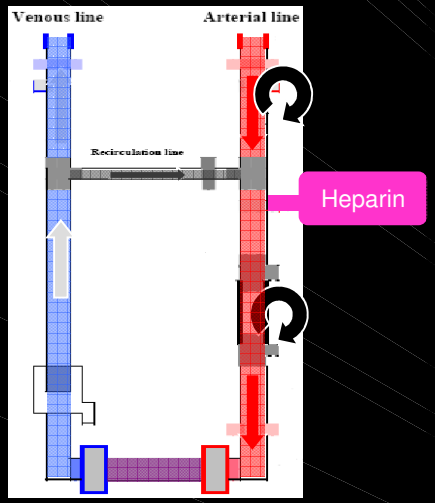


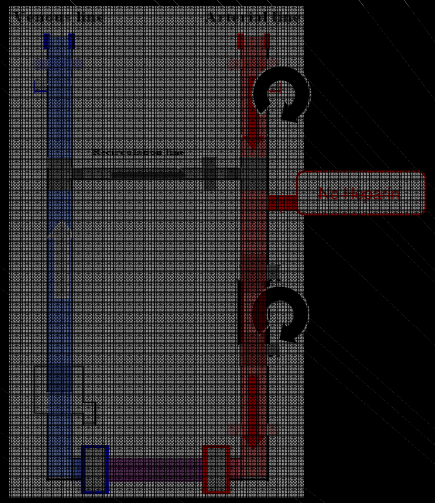
Stage 2a	Stage 2b	Stage 2c	Stage 2d
Routine heparin	Low heparin	No heparin	Routine heparin
mixed DNHD/AHD^{PR} sessions	*R-AHD^{PR}*	*R-AHD^{PR}*	DNHD sessions
	The PTT was widely fluctuating around the target PTT, as shown in the Figure:		

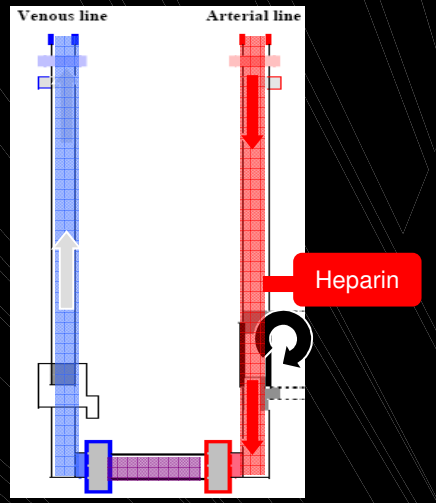


Results In R-AHD^{PR} sessions *(Stage 2)*







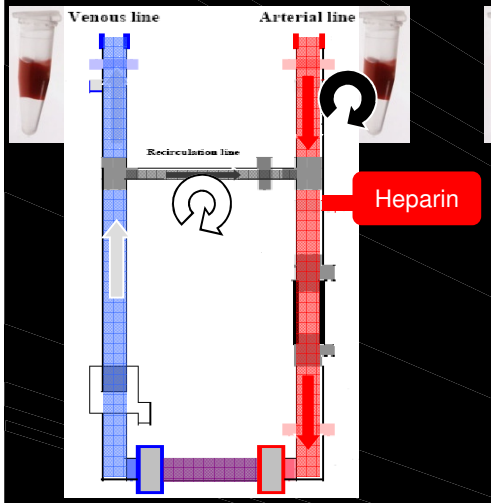


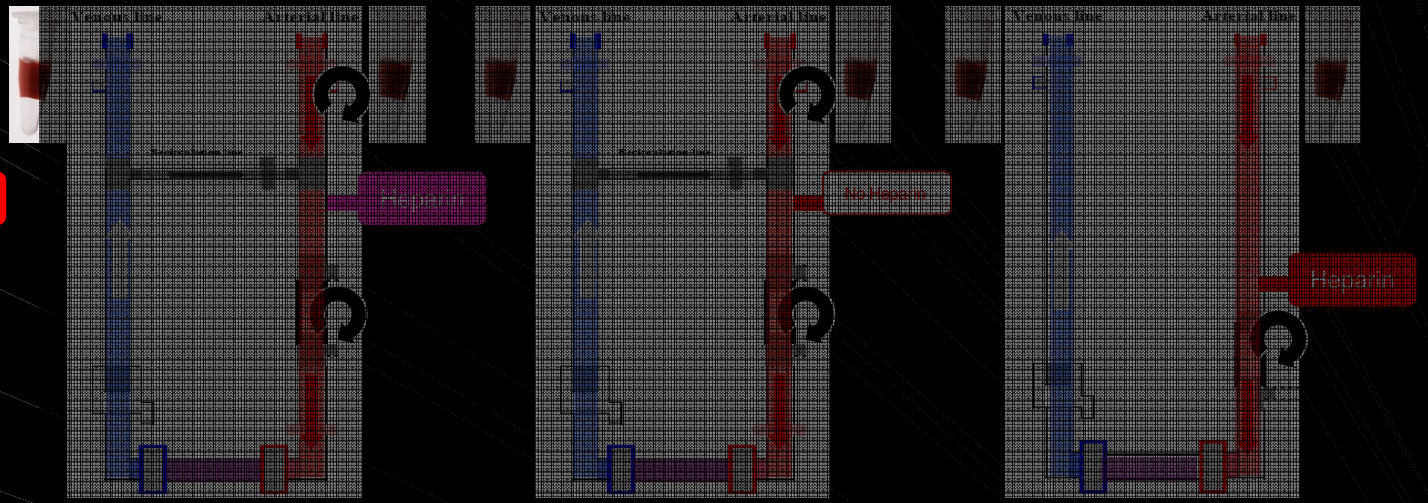
Stage 2a	Stage 2b	Stage 2c	Stage 2d
Routine heparin	Low heparin	No heparin	Routine heparin
mixed DNHD/AHD^{PR} sessions	*R-AHD^{PR}*	*R-AHD^{PR}*	DNHD sessions
	The mean dose of heparin used was 63.6 ± 17.4 Unit/kg		The mean dose of heparin used was 67.5 ± 15.1 Unit/kg

(P = 0.64

There was no significant difference between the mean dose of heparin used in **Stage 2b** compared to **Stage 2d (control)**.

Results In R-AHD^{PR} sessions *(Stage 2)*

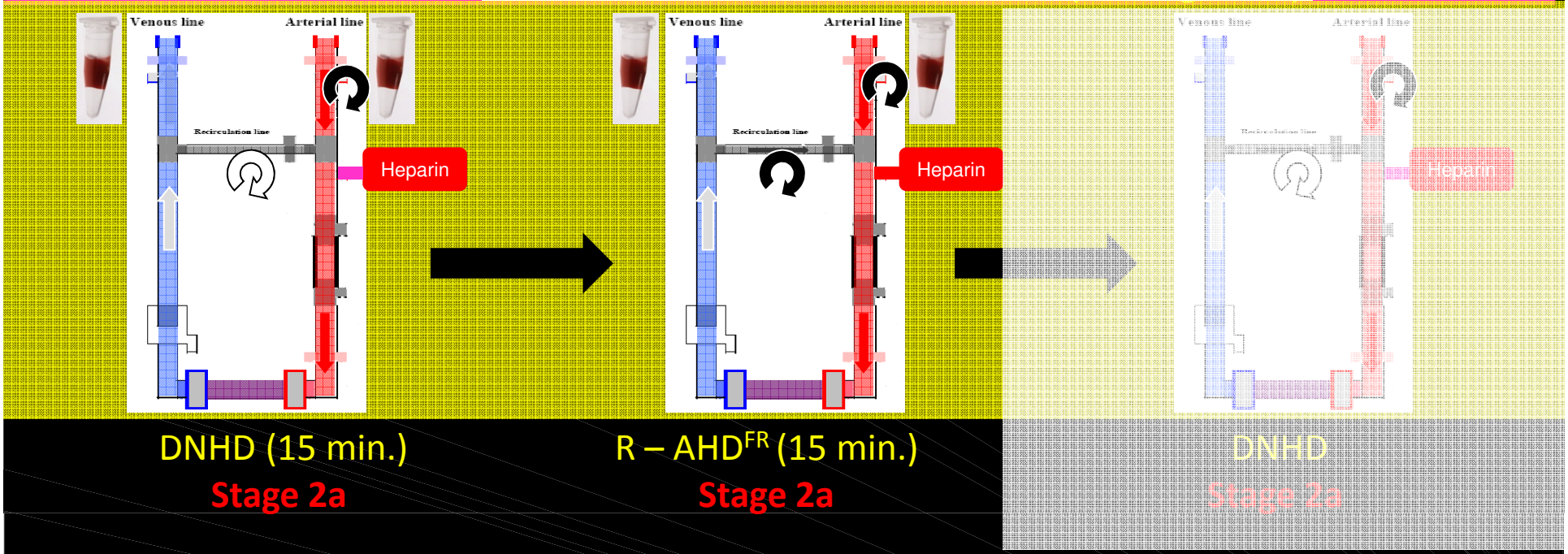




Stage 2a	Stage 2b	Stage 2c	Stage 2d
Routine heparin	Low heparin	No heparin	Routine heparin
mixed DNHD/AHD^{PR} sessions	*R-AHD^{PR}*	*R-AHD^{PR}*	DNHD sessions
F-URR was 0.6592 ± 0.15 after R-AHD^{PR} periods, compared to 0.79 ± 0.18 after DNHD periods . The mean difference was 0.13 ± 0.06 The 95% Confidence Interval of the difference ranged from - 0.005to 0.26			

(P = 0.059

Results In R-AHD^{PR} sessions *(Stage 2)*



DNHD (15 min.)
Stage 2a

R – AHD^{FR} (15 min.)
Stage 2a

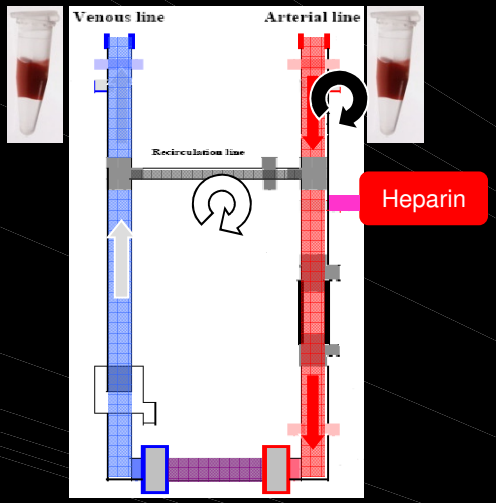
DNHD
Stage 2a

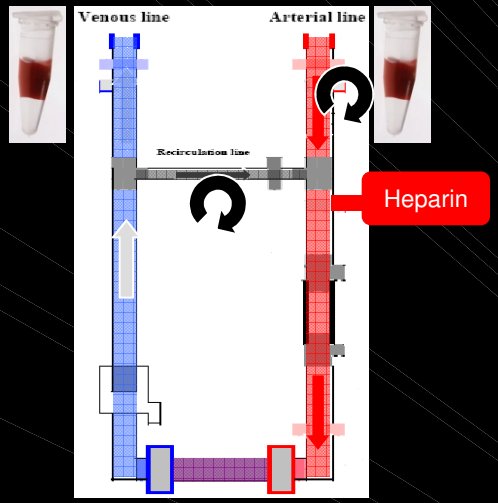
F-URR = 0.7869 ± 0.17722

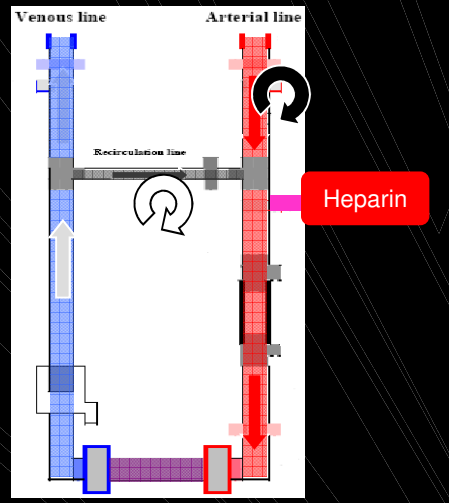
F-URR = 0.6592 ± 0.14555

F-URR was 0.6592 ± 0.14555 after R-AHD^{PR} periods, compared to 0.7869 ± 0.17722 after DNHD periods in *Stage 2a*. The mean difference was 0.12768 ± 0.06495 and the 95% Confidence Interval of the difference ranged from - 0.00536 to 0.26072 (P=0.059).

Results In R-AHD^{PR} sessions *(Stage 2)*





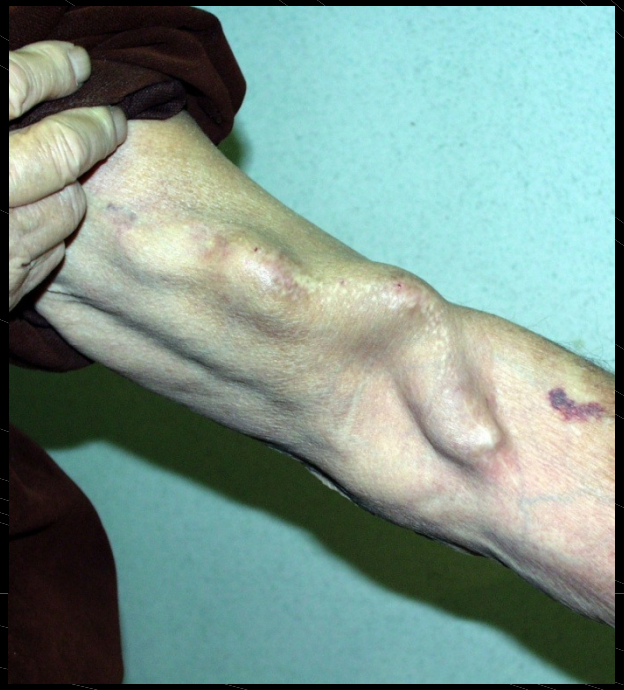


Stage 2a

After DNHD period	**After R-AHD^{PR} period**
F-URR = 0.7869 ± 0.17722	**F-URR = 0.6592 ± 0.14555**

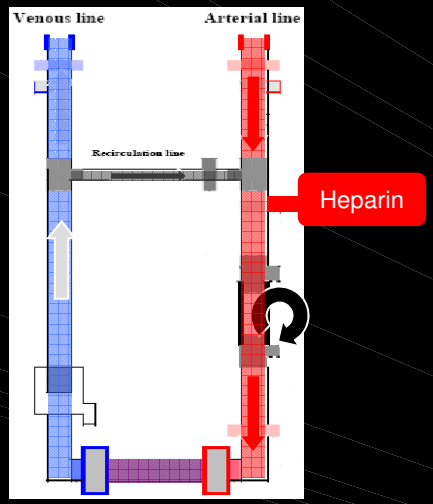
F-URR was 0.6592 ± 0.14555 after R-AHD^{PR} periods, compared to 0.7869 ± 0.17722 after DNHD periods in *Stage 2a*. The mean difference was 0.12768 ± 0.06495 and the 95% Confidence Interval of the difference ranged from - 0.00536 to 0.26072 (P=0.059).

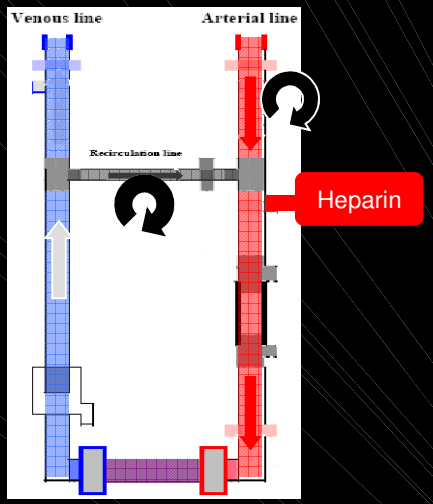
Results In R-AHD^{PR} sessions *(Stage 2)*



Neither Hypotension nor arterio-venous fistula complications were encountered nor were arterial pressure, venous pressure or blood leak alarms displayed on the hemodialysis machine monitor during the trial.

Results In R-AHD^{PR} sessions *(Stage 2)*

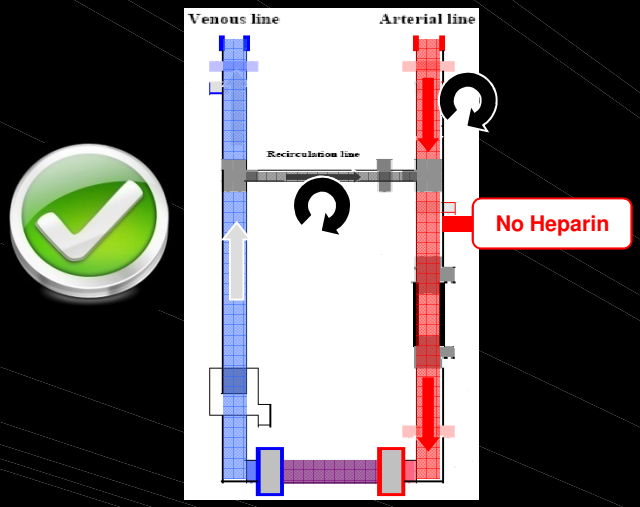




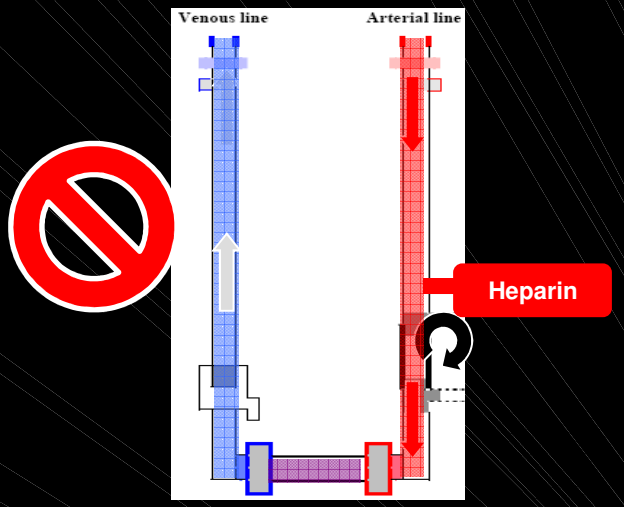
Children were more compliant to R-AHD^{0}, which was performed in the main dialysis room, compared to R-AHD^{PR} which was performed with an older hemodialysis machine in a smaller dialysis room.

Discussion

Discussion



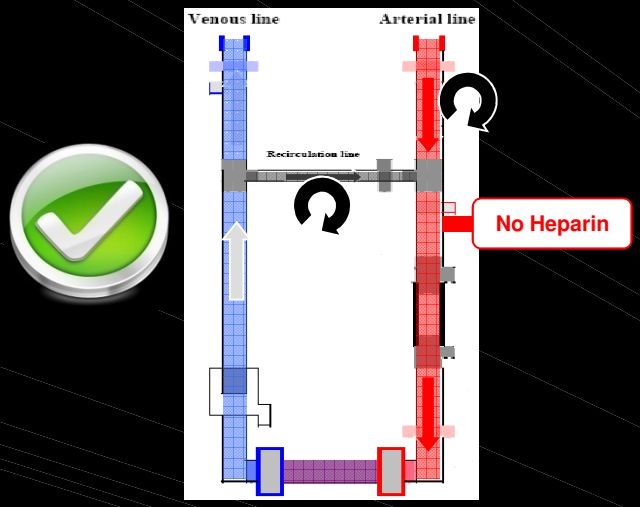
No heparin R-AHD^{PR}



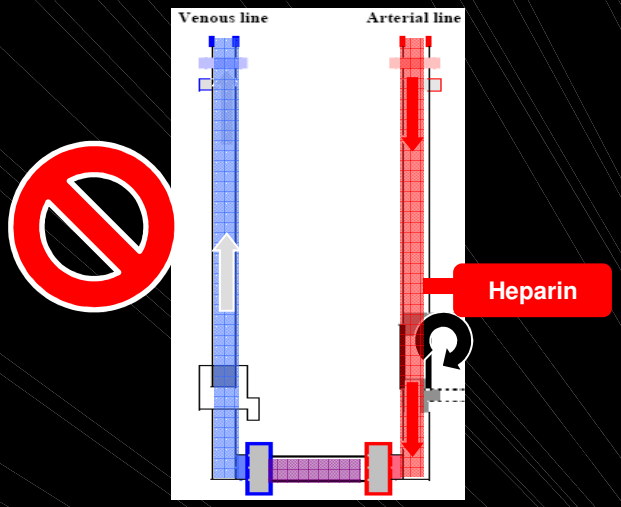
Routine heparin R-AHD^{0}

The current study emphasized the clinical feasibility of AHD. This was declared in the earlier study by El Hatw (1999) [6] where 10 R-AHD^{V} sessions and 5 S-AHD^{V} were carried on for one girl and the problem of blood clotting was not detected and the technique was said to be safe .

Discussion



No heparin R-AHD^{PR}



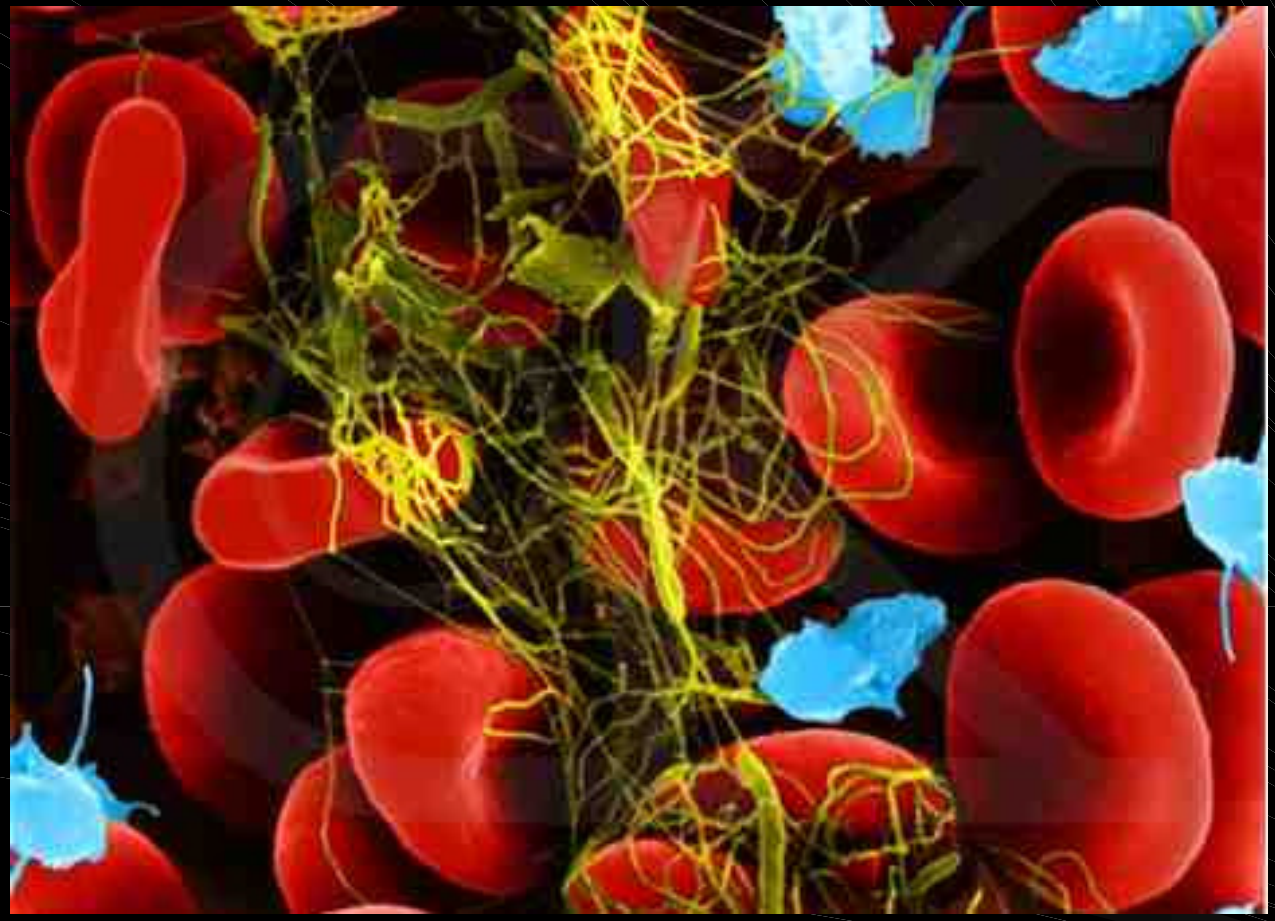
Routine heparin R-AHD^{0}

AHD models, differ in their ability to prevent extracorporeal blood clotting. AHD^{PR} in the safest model .

Discussion

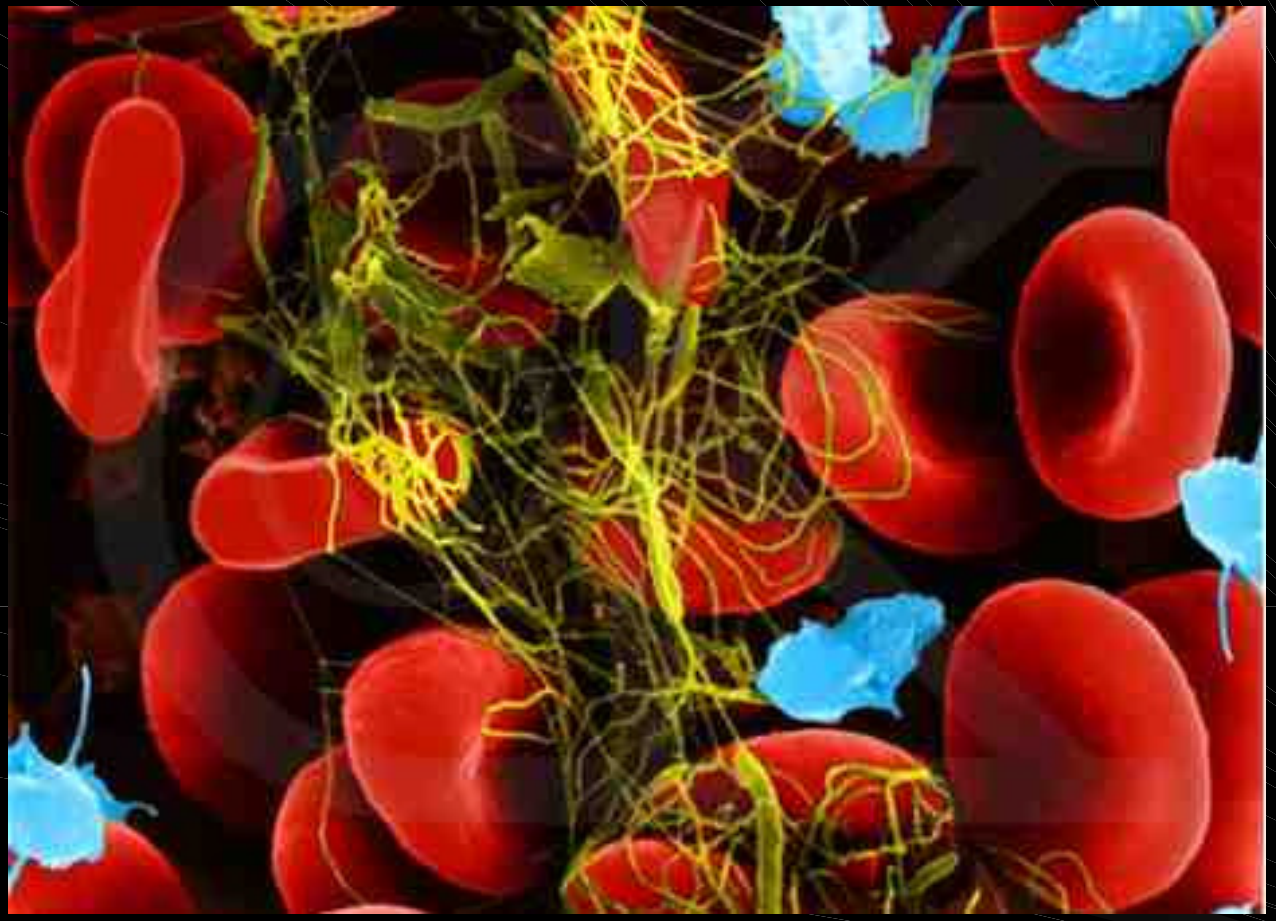
	$R\text{-}AHD^{0}$ sessions	$R\text{-}AHD^{PR}$ sessions
Blood clotting	Was observed even with Routine heparin dose.	Not observed in Routine, low or no heparin Sessions.
Efficiency	There was an insignificant decrease (not increase) of the efficiency compared to the DNHD.	
Anemia	Not observed even after a month of continuous $R\text{-}AHD^{0}$ sessions	None
AV fistula complications	None	None
blood leak problems	None	None

Discussion



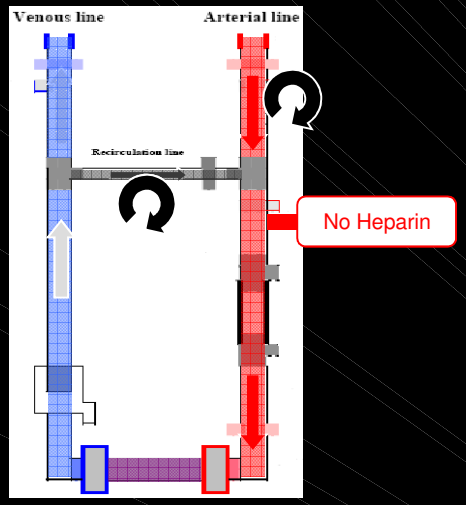
"Blood stasis is an essential factor in the formation of a haemostatic plug". [12]

Discussion



"No heparin R-AHD^{PR}" was carried out successfully for children with normal coagulation profile using a low patient BFR of 100 ml/min. Partial blood recirculation (PBR) selectively accelerates the BFR the intracircuit flow in the filter and the air trapping chamber, which are the widest and the most vulnerable points for clotting of blood, increases the shear forces in the capillary fibers, diminishes protein layering, and retards membrane clotting" [5]

Discussion



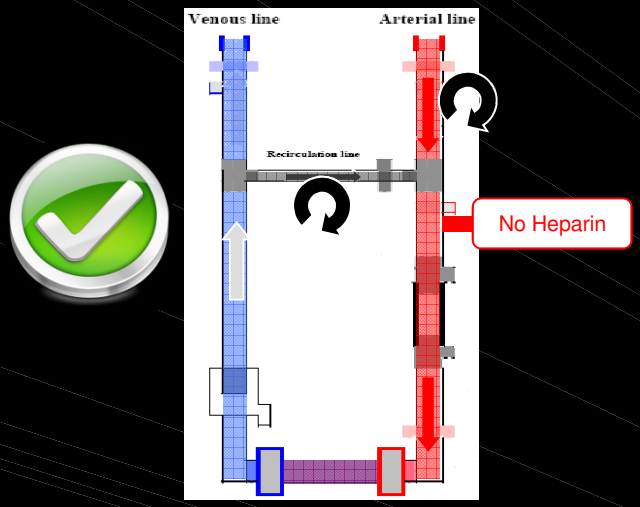
No heparin R-AHD^{PR}

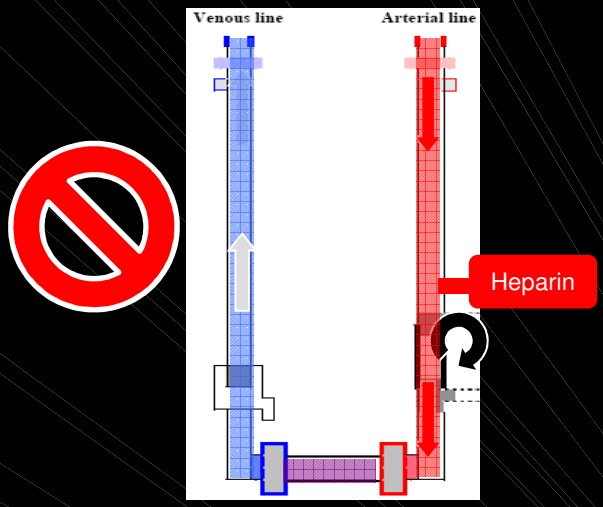
"No heparin R-AHD^{PR}" is a promising mode for avoiding blood clotting in hemodialysis.

It spares cost and complications of heparin and the cost of adding the (R) with 2 "T" shaped connections at its ends used to construct AHD^{PR} connections was minimal.

It is superior to other modes of dialysis.

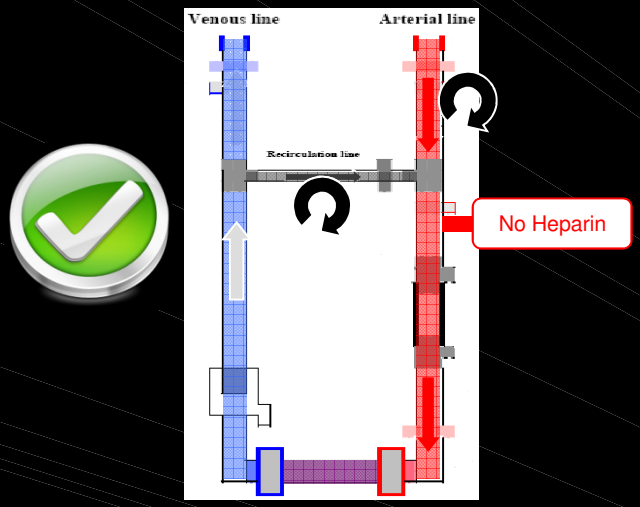
Discussion

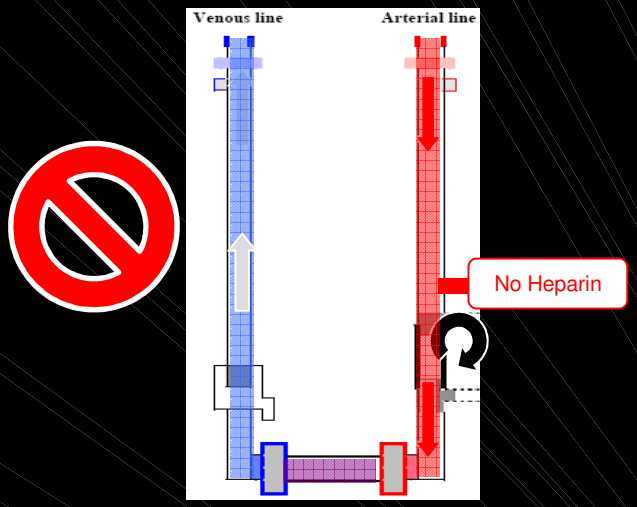




No heparin R-AHD^{PR}	Routine heparin DNHD
Spares the cost and the potential complications of heparin.	Cost and the potential complications of heparin.

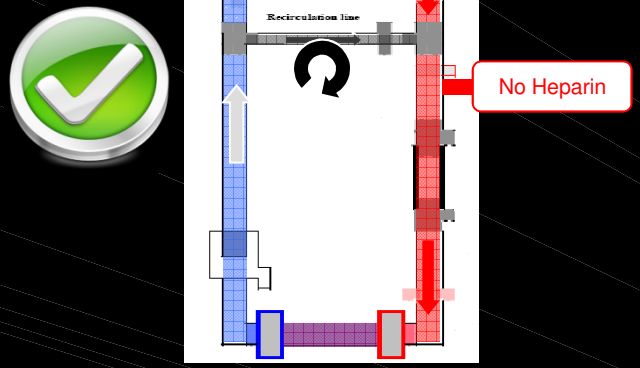
Discussion

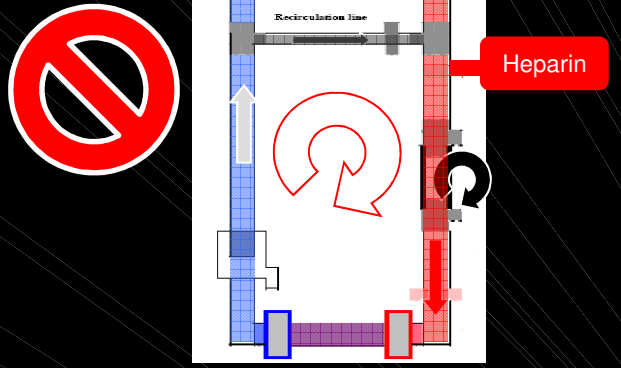




No heparin R-AHD^{PR}	No heparin DNHD
Does not need increasing the patient blood flow	Needs a patient blood flow rate of at least 300 ml/min.

Discussion

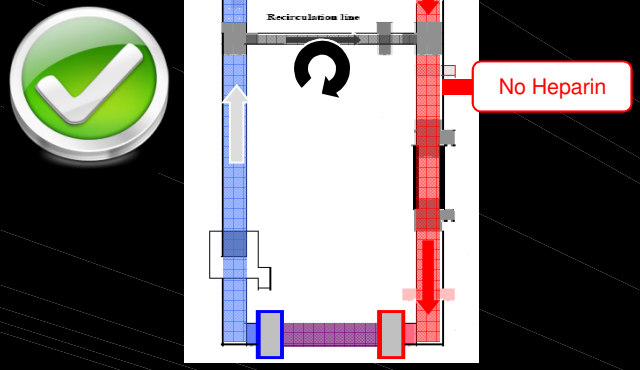


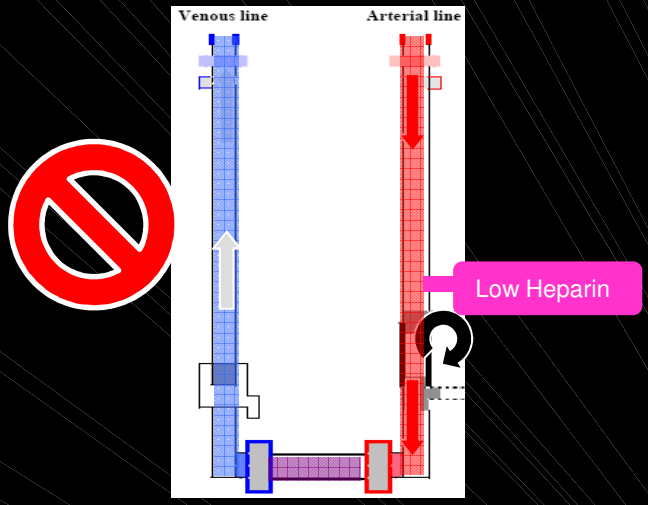


No heparin R-AHD^{PR}	Routine heparin R-AHD^{0}
Can detect accidental obstruction of the venous line: • Creates a negative venous pressure at the venous pressure monitors • Produce the audible sheering sound of the blood pump that alerts the operator to fix the problem	The single blood pump can not accurately adjust and maintain the patient BFR. Lacks alarm if the venous fistula is accidentally obstructed.

In our study, blood clotting was not due to hypercoagulable blood *"Routine heparin R-AHD^{0}* as the clotting time was normal or high before the sessions. Although clotting occurred in the early sessions of the *Stage 1c* where a dry fistula needle was used and not in the later sessions when needles were flushed with heparinized saline, yet the results were not encouraging for proceeding to the *"low heparin R-AHD^{0}"* and *"no heparin R-AHD^{0}"* Stages.

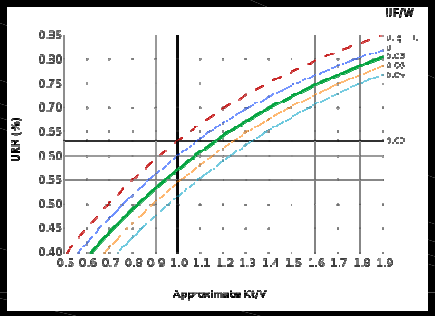
Discussion

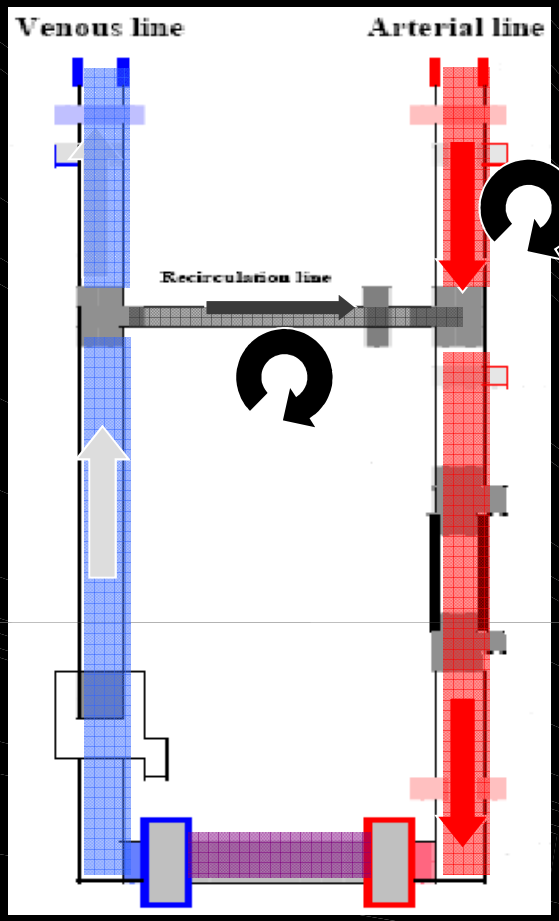




No heparin R-AHD[PR]	Low heparin DNHD
Technically easy Does not need sophisticated bedside laboratory monitoring.	Needs a bedside PTT monitoring, which is: • **Costly** as it needs a coagulometer, a centrifuge and a trained personnel. • **Risk of Anemia & infection** from repeated sampling. • **Inaccurate** as the PTT was widely fluctuating around the target PTT • **Ultimately useless** as reduction of the total dose of heparin/kilogram body weight was insignificant, *where a smaller dose of heparin was infused through out the session*, **compared to the *"Routine heparin sessions"* where heparin was discontinued in the last hour of the session.**

Discussion





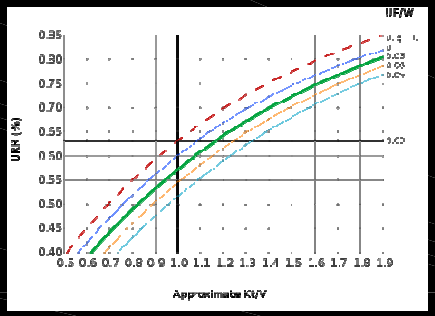
BFR to & from the patient

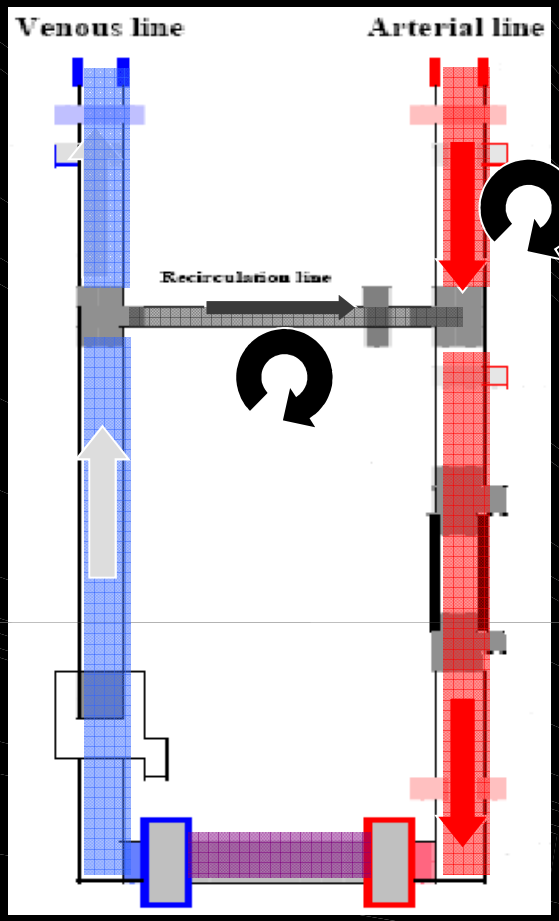
Filter BFR

R - AHD^{PR}

"The possibility that the rapid filter BFR in R-AHD will increase the dialysis efficiency and decrease the dialysis session time was attractive but actually PBR was associated in both R-AHD^{0} and R-AHD^{PR} with insignificant decrease in the hemodialysis efficiency, indicating that the efficiency depends on the BFR to & from the patient not on the filter BFR.

Discussion





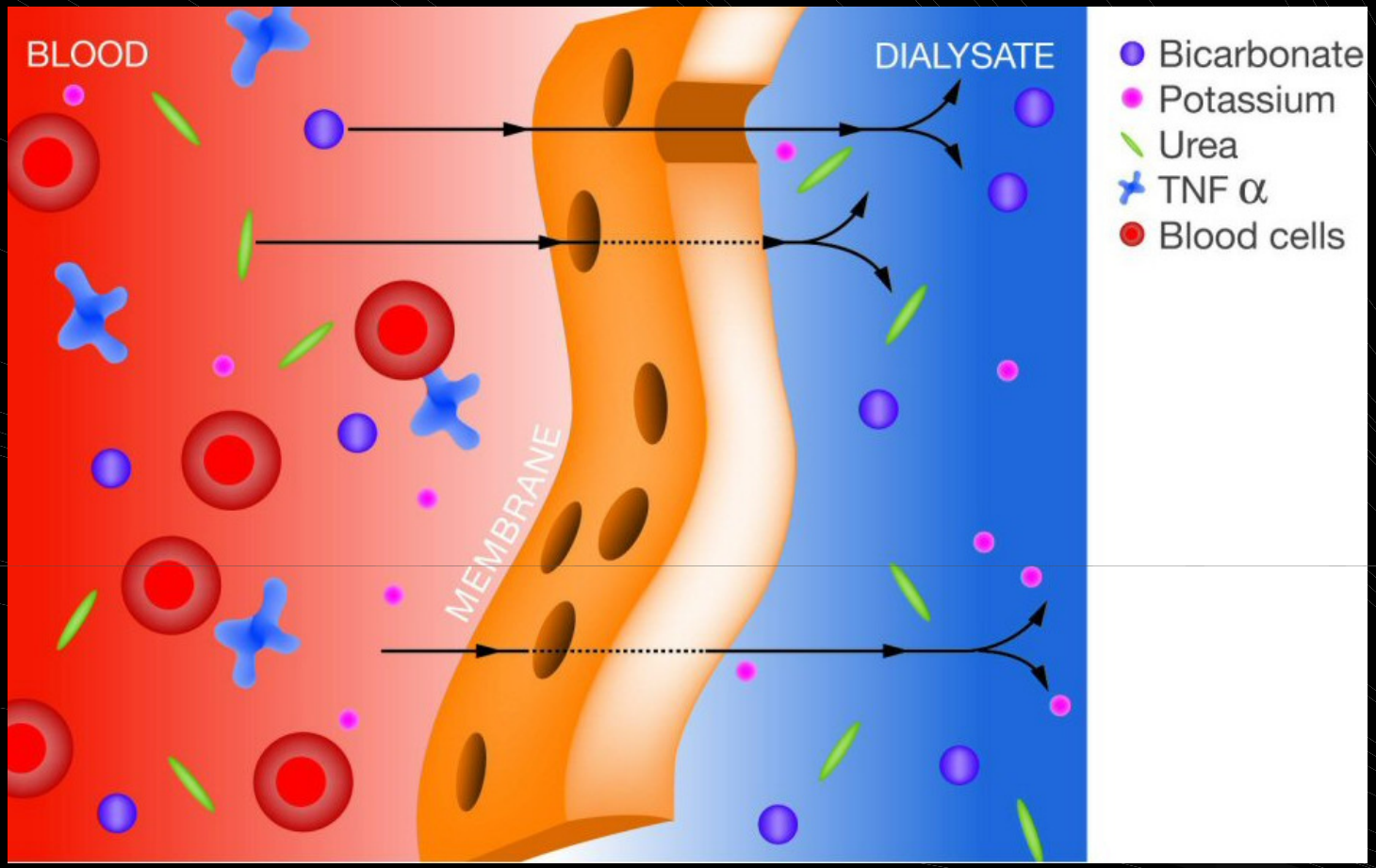
BFR to & from the patient

Filter BFR

R - AHD^{PR}

Increasing the filter BFR in R-AHD (both R-AHD^{0} and R-AHD^{PR}) did not increase the dialysis efficiency. The efficiency depends on the BFR to & from the patient not on the filter BFR.

Discussion



PBR was associated with insignificant decrease in the hemodialysis efficiency, possibly due to influx of uremic toxins from the dialysate to the recalculating blood in the filter. Increasing the dilayste flow rate may prevent this possible influx and improve the efficiency.

Discussion

4 hours

4 hours

4 hours

Sunday

Monday

Tuesday

Wednesday

Thursday

Friday

Saturday

2 hours

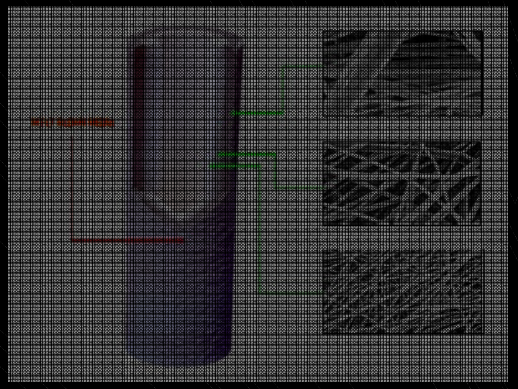
2 hours

2 hours

2 hours

2 hours

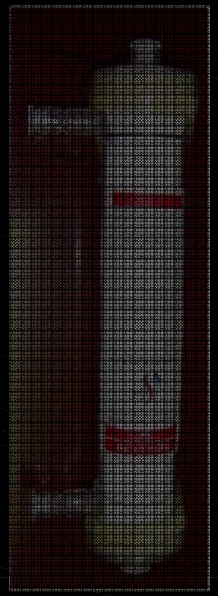
2 hours

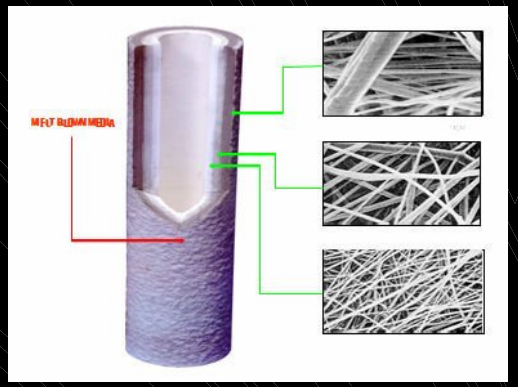


Anyhow,

- Increasing the dialysis efficiency in the traditional chronic hemodialysis sessions that are carried for 4 hours, three times per week is of limited value as the target efficiency can be achieved by the commercially available filters.

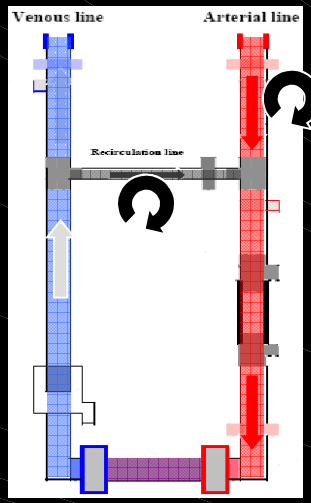
Discussion



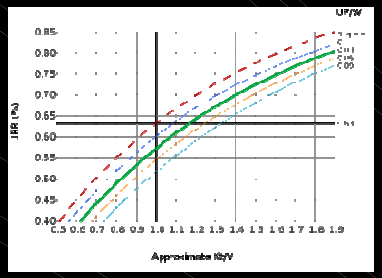


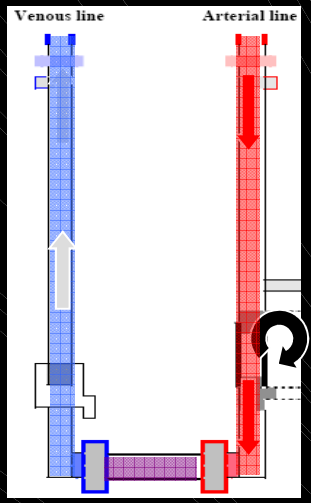
- The use of high flux filter remains the recommended approach if the efficiency is a concern as in daily dialysis where 2 hours sessions are carried out 5-6 days every week.[13, 14]

Discussion



AHD

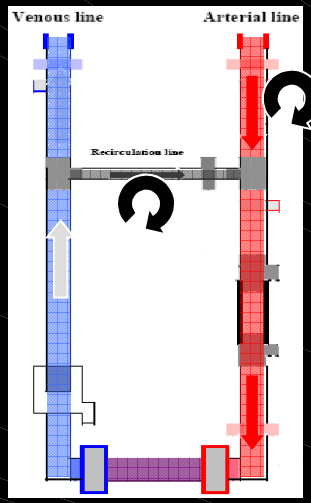




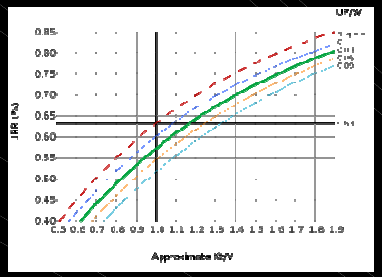
DNHD

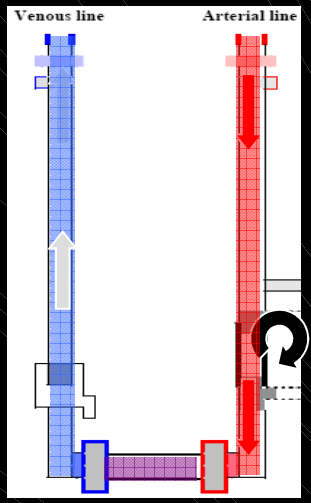
The results on effect on efficiency in the current study is compatible with the results of an earlier study by El Hatw on 1999 [6] who stated that "The efficiency of AHD was not increased by increasing the filter BFR in both pediatric and adult filters".

Discussion



AHD



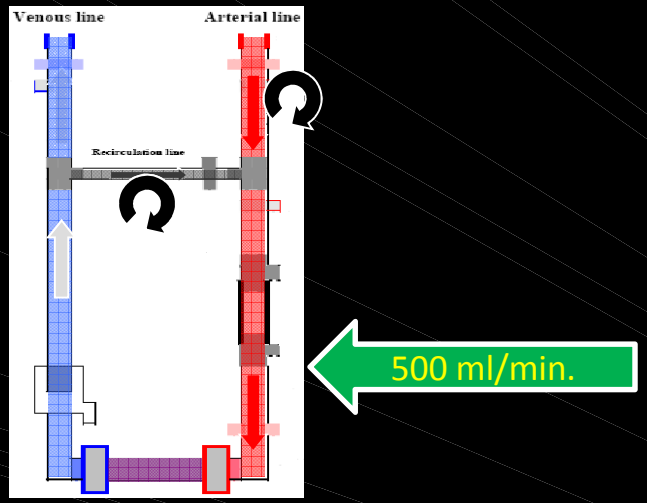


DNHD

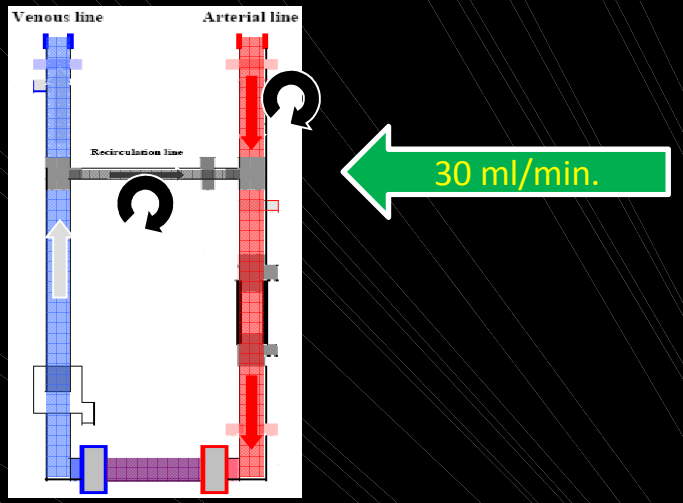
Yuji, (2008) [5] reported that “the clearance of solutes calculated either with or without PBR, was not substantially different with and without PBR".

Another clue that the efficiency of the AHD depends on the patient BFR rate, not the filter BFR rate, was that in S-AHD, efficiency decreased with the decrease of patient BFR[6] and that in Long sessions of S-AHD, the slow patient BFR decreased the efficiency per unit time and prevented over-dialysis in the long, 8 hours, hemodialysis sessions. [7].

Discussion



Our Study
(2005)



Yuji et al
(2008)

Yuji et al (2008) [5] used a low recirculation rate of 30 ml/minute as they were "afraid that PBR might increase the intracircuit pressure".

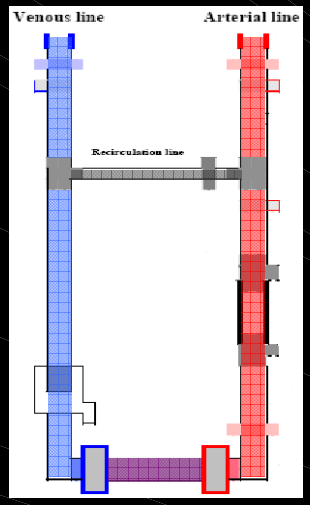
In our study blood recirculation was adjusted to achieve a filter BFR of 500 ml/minute with no mechanical drawback on the hollow fibers, the arteriovenous fistula or the integrity of the RBCs, issues that worried the reviewers of the proposal of the project. This goes with the experience in adult hemodialysis that is routinely carried out with a high BFR of 400-500 ml/ minute.

Yuji et al (2008) [5] reported a similar result that the hemogram did not show any significant differences whether PBR was used or not.

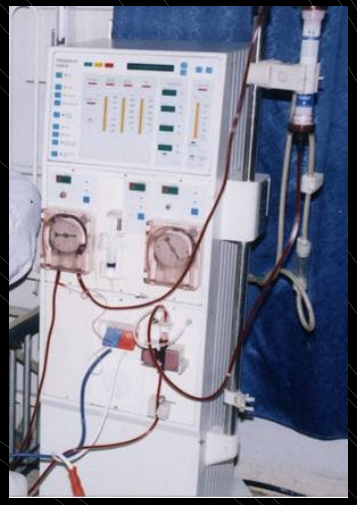
Discussion

The "no heparin R-AHD^{PR}" is a promising strategy of no heparin hemodialysis in children in whom achieving a fast BFR is not possible with the traditional hemodialysis sessions. More cases have to be studied before its recommendation in clinical practice. Financial and logistic difficulties limited number of the studied *"no heparin R-AHD^{PR}"* sessions in this study. *"No heparin R-AHD^{PR} "*sessions were the last Stage to be studies when the budged was exhausted and were carried out using an old version calibrated double blood pump Fresenius 2004B® hemodialysis machine that was about to be condemned from the unit that were fixed in the small and "unpleasant" acute hemodialysis room where trials for entertainment were not fruitful to attract the children. These confounding factors affected the compliance of children to the R-AHD^{PR}, compared to R-AHD^{0}, where 2 of the 10 patients skipped Stage 2b and only one child accepted to be maintained on R-AHD^{PR} for 10 continuous sessions.

Discussion



"R-AHD^{PR}

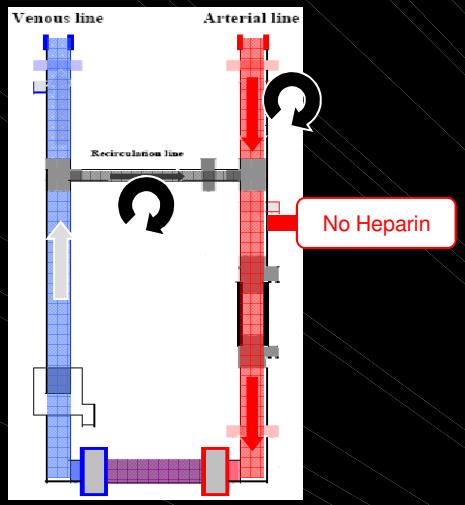


Double Pump HD machines

To test reproducibility of the study and for further studies on R-AHD^{PR},

- The corresponding author is willing to arrange in the supply of the AHD^{PR} connections.
- Most hemodialysis machines can be modified to be used in R-AHD^{PR} without changing its software by adding a 2nd blood pump, for around 3000 $, and directly connect it to the Alternating Current outlet.

Discussion

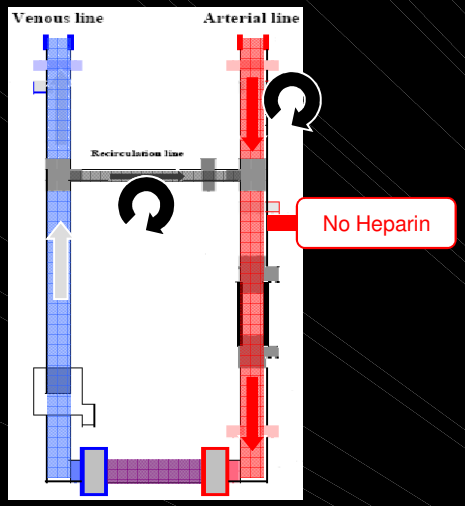


"No heparin-AHD^{PR} X higher number

Potential fields for further studies on *R-AHD^{PR}* includes

(1) Study a bigger number of *"no heparin R-AHD^{PR}"* children and adults for a longer period.

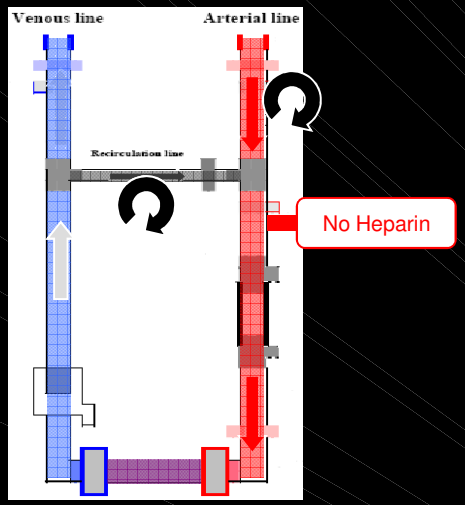
Discussion



"No heparin-AHD^{PR} + No Flush

(2) Study *"no-flush no-heparin R-AHD^{PR}"* to rule out the role of the concomitant flushing of the lines with saline in the inhibition of the blood coagulation. *"No-flush No-heparin R-AHD^{PR}"* can be used even in patients without bleeding tendency to spare the potential complications of heparin and spares cost of heparin and the saline flush

Discussion

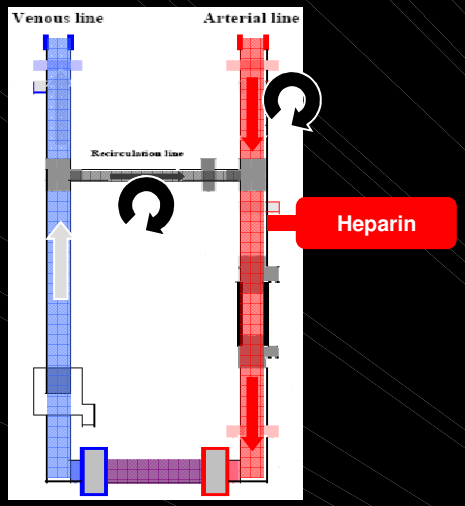


"No heparin-AHD^{PR} + S-AHD^{PR}"

(3) Study a combination of *"no heparin-AHD^{PR} and S-AHD^{PR}"* where

1. The filter BFR is increased to avoid clotting whereas
2. The patient BFR is decreased simultaneously Study Patient BFR less than 100 ml/ minute. to fit patients with low body weight, compromised cardiac function or poor vascular access or is very low as in continuous arteriovenous or venovenous hemofiltration or hemodialysis (CAVH/D and CVVH/D) as "the no heparin regiment is ineffective in this setting due to the low BFR rates with these techniques and their continuous nature increases the likelihood of side effects with prostacyclin or protamine" [2].

Discussion



"R-AHD^{PR} + High dialysate flow rate + Big filter

(4) Study the effect of *"R-AHD^{PR}"* with high dialysate flow rate and with bigger filters on the efficiency. Bigger filters will still increase the extra corporeal blood compartment, but PBR increase the BFR per single hollow fiber to prevent blood stagnation.

Conclusion

Conclusion

R-AHD^{PR} allowed successful low heparin and no heparin hemodialysis in children without increasing the patient BFR but did not increase the efficiency.

Conclusion

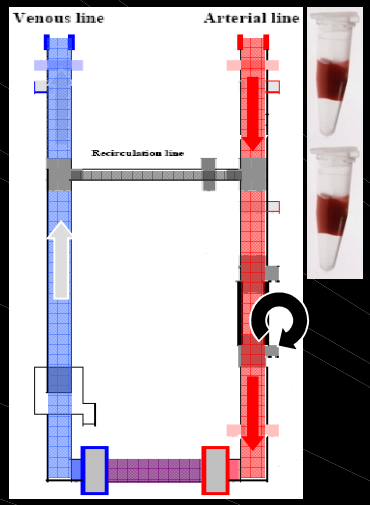
It is concluded that

(1) "no heparin R-AHD^{PR}" is an applicable and safe hemodialysis method in children

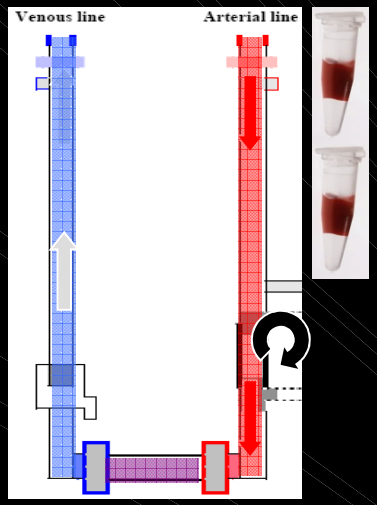
(2) R-AHD does not increase dialysis efficiency.

Thank you

Methods - *Setting and Study design*



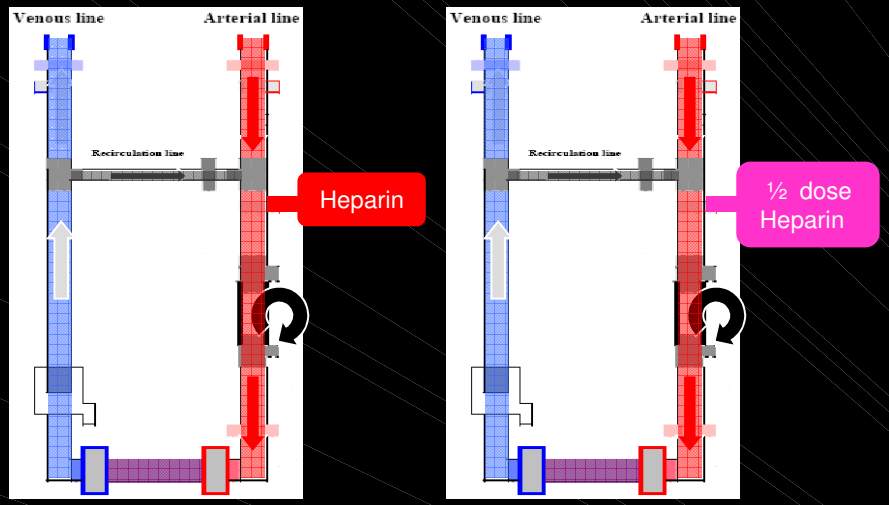
R-AHD^0
Stage 1a,b



DNHD
Stage 1d

(A) Efficiency of the AHD: Was measured by comparing the URR in R-AHD^0 (Stage 1a,b) and in DNHD sessions (Stage 1d) measured in the same patient. URR carries a possibility errors in calculating efficiency due to errors in post dialysis sampling or due to residual renal function.

Methods - *Setting and Study design*



Routine heparin
R-AHD^0
Stage 1a

½ dose heparin
R-AHD^0
Stage 1b

(B) Anticoagulant effect of the AHD was studied by comparing the "Routine heparin R-AHD^0" and "½ dose heparin R-AHD^0" sessions. The long clotting time before starting the sessions indicates that the used "Routine dose heparin was actually a "high dose" of heparin with a prolonged residual anticoagulant effect.