Adacolumn®

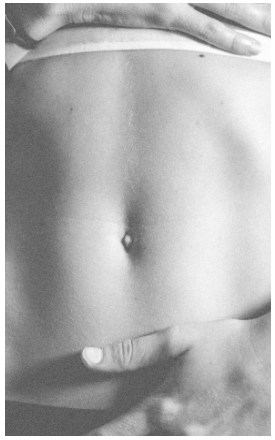
ADAMONITOR® SC

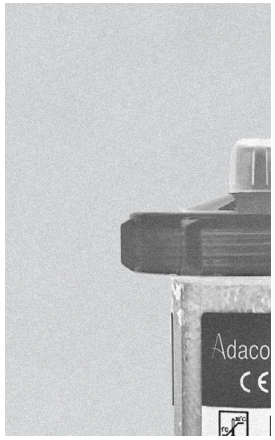
User manual

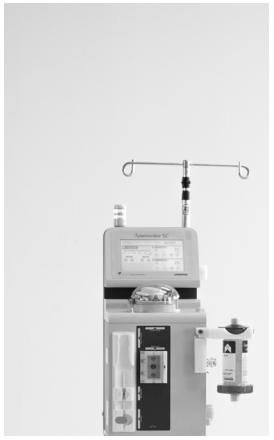
Adacyte Therapeutics

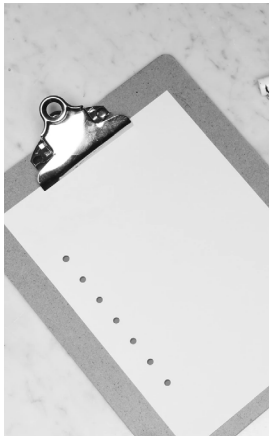
EN-ADA-1120042

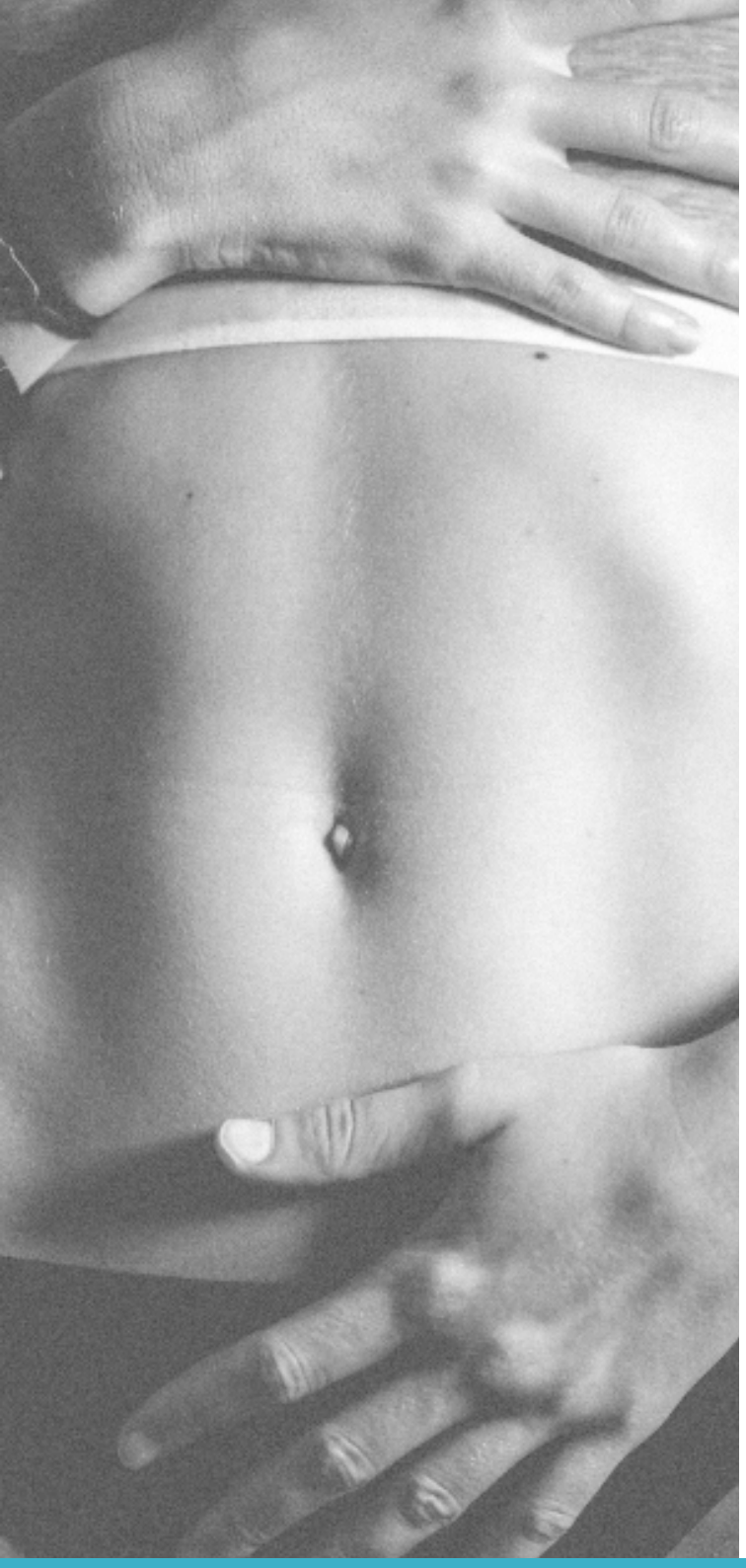
INDEX











01

Basic concepts of inflammatory bowel disease (IBD)

1.1 BASIC CONCEPTS ABOUT IBD

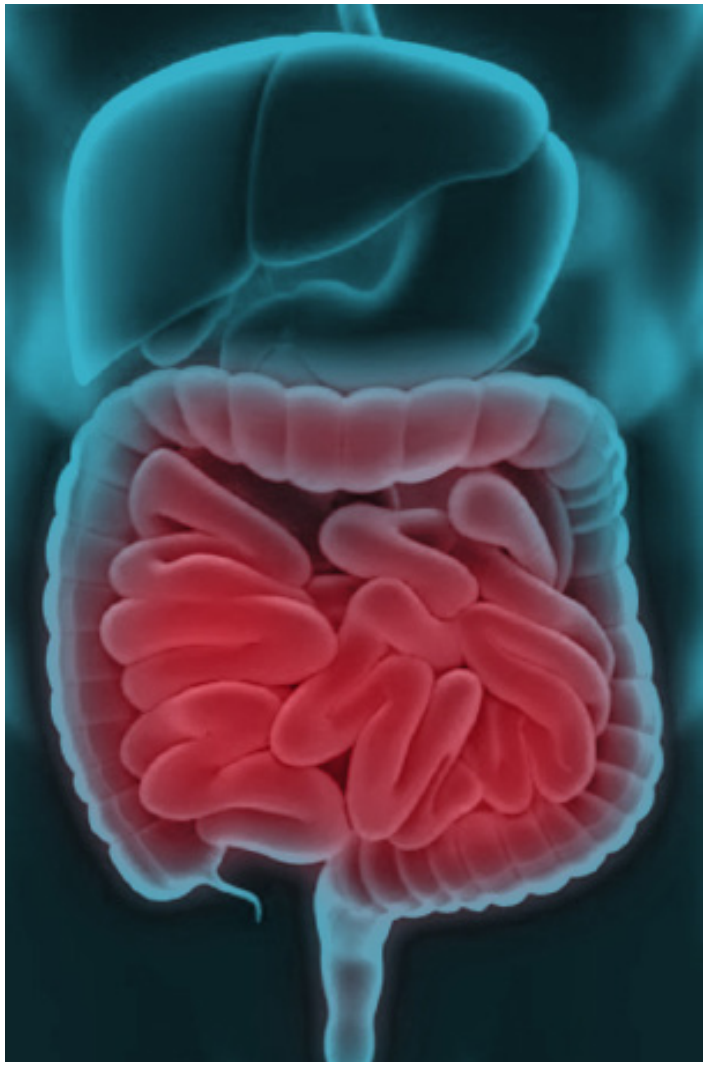
Inflammatory bowel disease (IBD) is a generic term that describes disorders that involve **chronic inflammation of the gastrointestinal tract** in different locations.

Chronicity during the course of IBD consists of alternating periods of inactivity that are identified as phases of **remission** along with periods of clinical activity of varying intensity called **flares or relapses**.

There are two main types of IBD:

- Crohn's disease (CD)
- Ulcerative colitis (UC)

These two diseases are very similar and it is sometimes even difficult to differentiate between them.
There is a third classification known as indeterminate colitis, when the characteristics cannot be determined and the final diagnosis will depend on its evolution.



1.2 ULCERATIVE COLITIS (UC)

Definition:

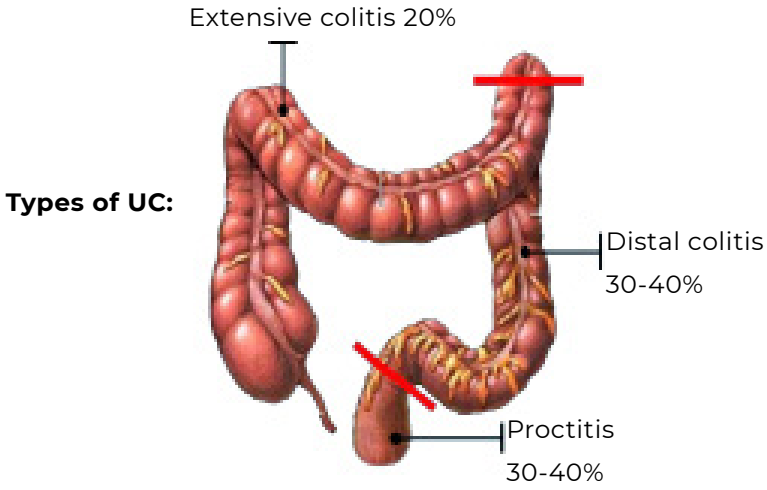
A type of chronic IBD that **diffusely affects the mucosa of the colon**, causing **long-term inflammation and sores** (ulcers) on the deeper lining of the large intestine (colon) and rectum. Inflammation usually begins in the rectum and extends proximally in continuity towards the cecum, stopping abruptly at the ileocecal valve.

Types of UC:

- Extensive colitis:
  Also called pancolitis, extends beyond the splenic flexure. Its treatment must be systemic and carries a higher risk of serious outbreaks and long-term colectomy.

- Distal or left-sided colitis:
  Its extension is distal to the splenic flexure. Its treatment can be approached by systemic and/or topical means in the form of an enema or foam.

- Proctitis:
  Affects the rectum or even the rectosigmoid junction. Its treatment can be approached by systemic and/or topical means in the form of an enema, foam or suppositories.



1.2 ULCERATIVE COLITIS (UC)

Symptoms:

- Alterations in the intestinal rhythm.
- Incontinence.
- Urgency to defecate.
- Tenesmus.
- Rectorrhagia: ulcerative colitis diarrhoea is usually associated with variable amounts of blood, which is often accompanied by mucus and sometimes pus.

Table 24-1 Outbreak activity according to the Montreal classification

(adaptation from [1])

Variable	Mild	Moderate	Severe
Number of bowel movements	≤ 4	5-6	> 6
Blood in stool	+	++	+++
Haemoglobin (g/l)	> 10.5	> 10.5	< 10.5
Fever	Not present	Not present	> 37.5 ° C
Heart rate	< 90	< 90	≥ 90
Erythrocyte sedimentation rate	< 30	< 30	> 30

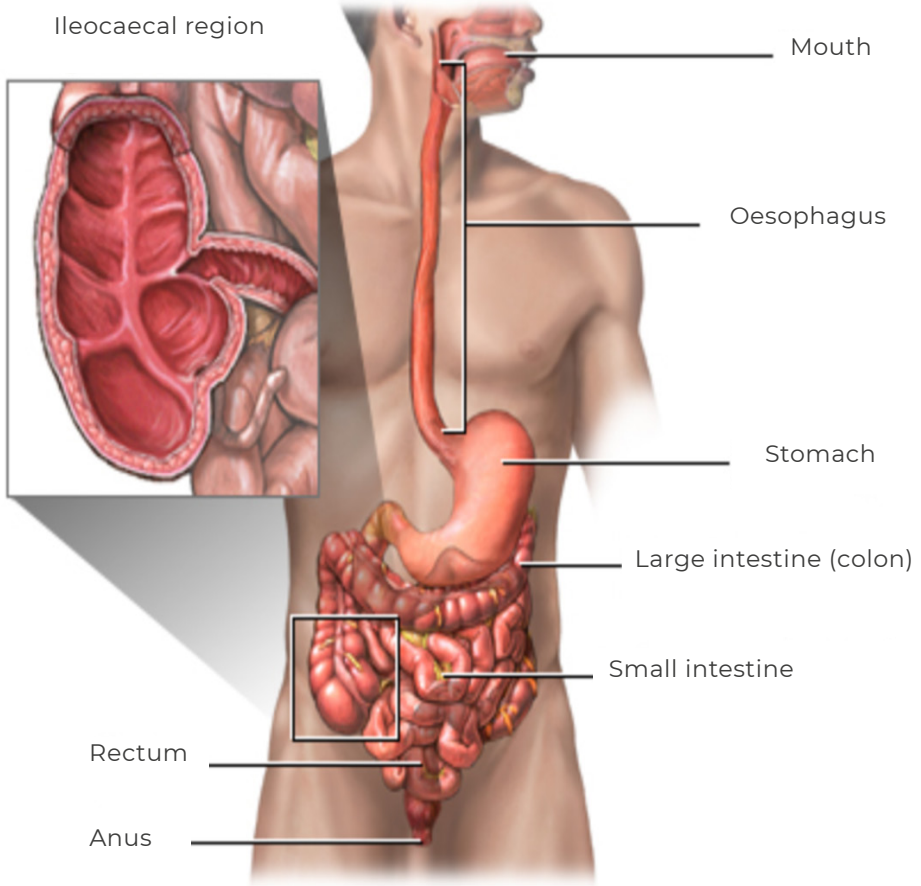
1 *Satsangi J. et al. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. Gut 2006;55:749–753. doi: 10.1136/gut.2005.082909*

1.3 CROHN'S DISEASE (CD)

Definition:

Type of chronic IBD that **can affect any area of the digestive tract,** from the mouth to the anus. The most common areas of disease are the terminal ileum and the cecum but it can affect only the rectum or even, much less frequently, the oropharynx.

CD usually presents a segmental inflammation which means that there are areas of the intestine that are preserved from the disease between the segments that are affected and that the length is variable. Furthermore, this inflammation is asymmetric along the circumference of the digestive tract and the different locations of the disease. CD is a transmural disease, therefore the inflammation can affect all layers of the intestinal wall.



1.3 CROHN'S DISEASE (CD)

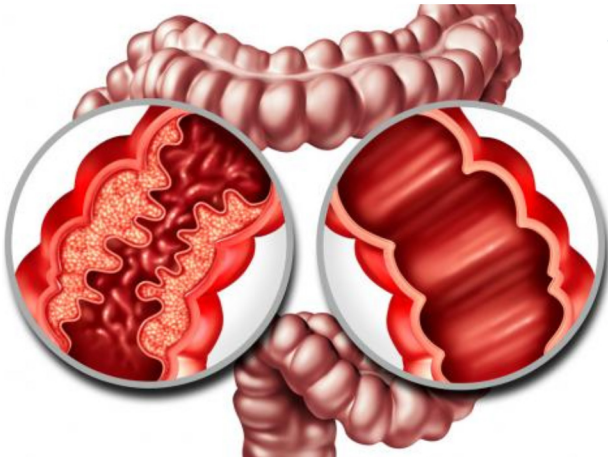
Symptoms:

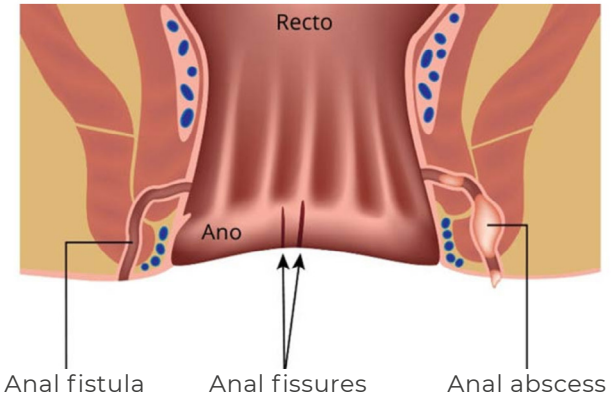
The symptoms are quite variable, depending on which part of the digestive tract is affected. These can arise or recede and the most common are:

- Fatigue
- Abdominal pain
- Poor nutrient absorption
- Fever
- Moderate diarrhoea (4 to 8 bowel movements per day)

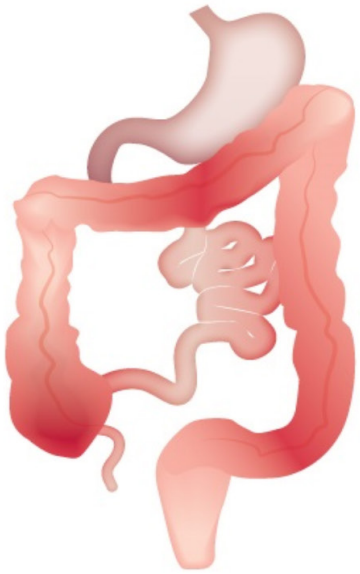
One third of the patients will be affected in the last section, the rectum and the anus, presenting frequent complications such as:

- Anal fissure
- Perianal fistula
- Perianal abscess



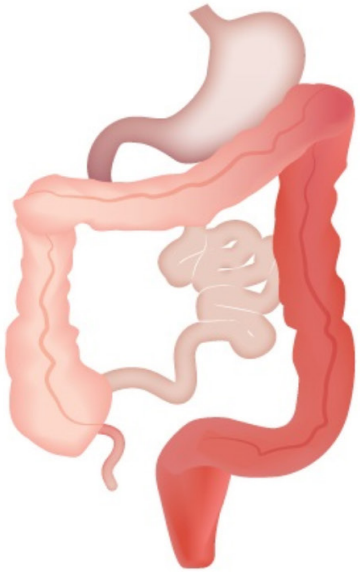


1.4 DIFFERENCES BETWEEN CD AND UC



Crohn's disease (CD)

- Affects rectum less frequently
- Any segment from the mouth to the anus
- Segmental and asymmetrical affection
- Fat wrap
- Development of fistulas and stenosis
- Perianal disease
- Intra-abdominal abscesses
- Serpiginous ulcers, cobblestone
- Healthy areas alternate with inflamed sections



Ulcerative colitis (UC)

- Rectal disorder
- Greater or lesser extent of the colon
- Continuity and symmetrical affection
- Thickening of the muscle layer
- Uncommon stenosis and fistulas
- Rare perianal disease
- Rare abscesses
- Loss of vascular pattern, oedema, ulcers
- The extent and severity of colon inflammation varies from person to person

02

Granulocyte-monocyte apheresis (GMA)

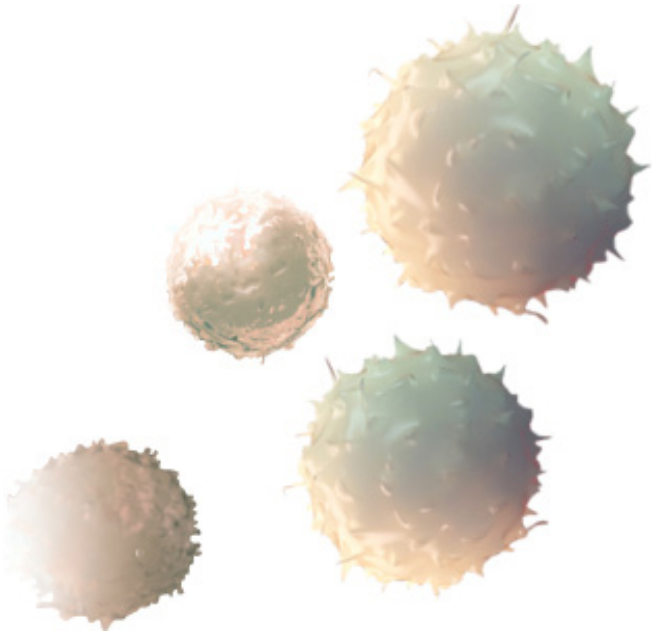
2 GRANULOCYTE-MONOCYTE APHERESIS (GMA)

GMA is a procedure that allows for removal of different active leukocyte populations from the blood and for the modification of mediators that intervene in the inflammatory process, **eliminating the granulocytes and monocytes that cause tissue damage from the organism.**

Due to this and its theoretical **immunomodulatory effect**, it represents an attractive option for the treatment of Inflammatory Bowel Disease.

Patient profiles for which GMA has proven to be effective include:

- Steroid-dependent patients.
- Special populations (vulnerable patients: advanced age, comorbidities, intolerance to immunosuppressive or biological treatments, history of neoplasia...).
- Bridge treatment to Immunosuppressants or Vedolizumab.
- Combination with ANTI-TNF in case of partial response or loss of response.



Prodiggest Project rational use of granulocytopheresis in inflammatory bowel disease

Shimoyama T, Sawada K, Hitwatasi N, Sawada T, Matsueda K, Munakata A, et al. Safety and efficacy of granulocyte and monocyte adsorption apheresis in patients with active ulcerative colitis: a multicenter study. J Clin Apher. 2001; 16: 1-9

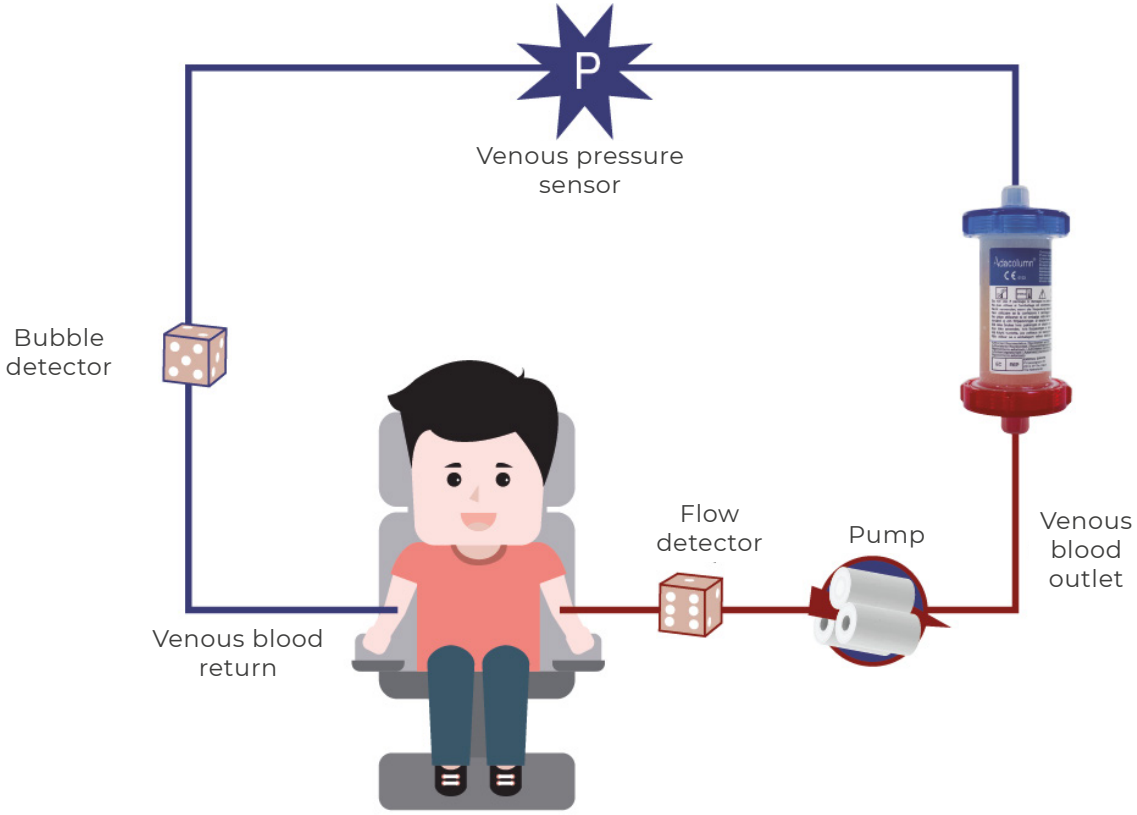
Hanai H, Takeda Y, Lofberg R. The mode of actions of the Adacolumn® therapeutic leucocytapheresis in patients with inflammatory bowel disease: a concise review. Clin Exp Immunol. 2011; 163: 50-58.

Cabriada JL, Doménech E, Gomollón F, González-Carro P, González-Lara V, Hinojosa J, et al. Consensus document on the use of granulocytoapheresis in patients with inflammatory bowel disease. Gastroenterol Hepatol. 2006; 29(2): 85-92.

2 GRANULOCYTE-MONOCYTE APHERESIS (GMA)

What is the process?

After the blood is extracted, preferably through one of the antecubital veins, and passes through the circuit and the ADACOLUMN ® filter, it is re-infused into the patient through one of the contralateral antecubital veins.



- 335ml column filled with 220g of cellulose acetate beads with a diameter of 2mm.
- Selective adsorption of granulocytes and monocytes/macrophages.

- Session duration: 60 min.
- Flow: 30 ml/min.
- Anticoagulation with Heparin.
- Haemodialysis unit/ apheresis unit.
- Peripheral vein procedure

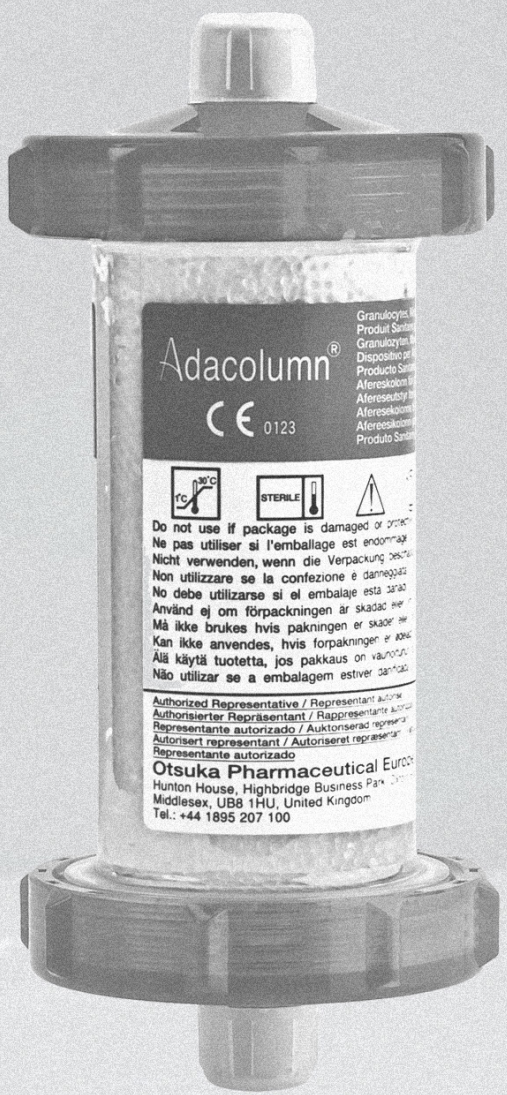
Yamamoto T,Umegae S, Matsumoto K. Safety and clinical efficacy of granulocyte and monocyte adsorptive apheresis therapy for ulcerative colitis. World J Gastroenterol. 2006 Jan 28; 12(4): 520-5

** Some authors have shown better results with longer exposures (90 min.). N. Yoshimura, T. Tadami, T. Kawaguchi, M. Sako, H. Yoshimoto, T. Yamaka, et al. Processed blood volume impacts clinical efficacy in patients with ulcerative colitis undergoing adsorptive depletion of myeloid lineage leucocytes. J Gastroenterol., 47 (2012), pp. 49-55.*

RATIONAL USE OF GRANULOCYTOAPHERESIS IN INFLAMMATORY BOWEL DISEASE

TABLE 5. RECOMMENDED APHERESIS GUIDELINES

Number of sessions:	Guideline of 5 to 10 sessions (assess age refractory to other treatments).
Frequency:	Two sessions per week, at least during the first 2-3 weeks. If this increase in frequency is not possible, use the standard guideline of 1 session per week.
Filtration flow:	Regular flow: 30 ml/min.
Length of sessions:	Flows of 40 ml/min or 50 ml/min are more difficult to achieve and depend on the venous access. A fixed time is not necessary, but at least 60 minutes at 30 ml/min is recommended.
Blood volume processed per session:	At least 1800 ml per session. Better results at higher percentage of circulating plasma volume (CPV) processed. If possible, filter 100% of CPV calculated according to Kaplan's formula. Circulating Plasma Volume (CPV) = [0.065 x Weight (kg)] x (1 - hematocrit).



03

Adacolumn®

3 ADACOLUMN®

Adacolumn®

Adacolumn® :

- Column **containing 220g of cellulose acetate beads bathed in physiological saline.** Each microsphere is approximately 2mm in diameter and has a rough surface to enhance its adsorption properties.
- Selectively **retains granulocytes** (65%) and **activated monocytes** (macrophages 55%) in order to **reduce the inflammatory process** caused by the presence of these cells in the blood.
- Adsorption occurs through the adhesion of activated granulocytes and monocytes to the cellulose acetate spheres.

Indications:

Adacolumn® is indicated for the treatment of the following autoimmune diseases:

- Induces remissions in patients with inflammatory bowel disease (active ulcerative colitis and Crohn's disease).
- Suppresses subjective and objective symptoms in patients with rheumatoid arthritis in inflammatory phase who may be resistant to standard drug treatment.
- Treats patients with ocular Behçet's disease.
- Treats patients with systemic lupus erythematosus (SLE).
- Improves clinical symptoms in patients with pustular psoriasis (PP).

Contraindications:

Adacolumn® should not be used in patients with a peripheral blood granulocyte count below 2000 granulocytes/µl.
In patients with a granulocyte count below this limit due to previous drug treatment, Adacolumn® may be used under close supervision as long as the granulocyte count is above 1000/µL. Studies in patients with SLE and a comparable granulocyte count did not show further reductions with Adacolumn® treatment.

Yamamoto M, Umegaes S, Kitagawa, Yasuda Y, Yamada Y, Takahashi D, T et al. Granulocyte and monocyte adsorptive apheresis of active distal ulcerative colitis. A prospective pilot study. Aliment Pharmacol Ther. 2004; 20: 783-792.
Yamamoto M, Umegaes S, Matsumoto K. Safety and clinical efficacy of granulocyte and monocyte adsorptive apheresis therapy for ulcerative colitis. World J Gastroenterol. 2006; 12: 520-525.

Saniabadi AR, Hanai H, Takeuchi K, Umemura K, Nakashima M, Adachi T, Shima C, Bjarnason I, Lofberg R. Adacolumn®, an adsorptive carrier based granulocyte and monocyte apheresis device for the treatment of inflammatory and refractory diseases associated with leukocytes. Ther Apher Dial. 2003 Feb;7(1):48-59. doi: 10.1046/j.1526-0968.2003.00012.x. PMID: 12921115

For more information about the product, visit IFU at www.adacyte.com.

Disclaimer:

SPECIAL CAUTION should be taken for the following patients:

- That have or may have concomitant infections.
- With hypersensitivity to heparin.
- Particular caution should be exercised in patients with a low red blood cell count (less than 300 x 10^4 /mm ^{3}), severe dehydration (red blood cell count greater than 600 x 10^4/mm ^{3}) and hypercoagulability of the blood (fibrinogen greater than 700 mg/dL). Apheresis treatment should not be started until these parameters have normalised.
- With body temperature above 38°C.

It is recommended to NOT START treatment until values have normalised in:

- Patients treated with angiotensin converting enzyme inhibitors (ACE Inhibitors): monitor blood pressure and heart rate.
- In patients with severe cardiovascular disease, the attending physician will carefully assess the benefits or risks of Adacolumn® treatment.
- Patients with liver or kidney failure, or severe cardiovascular disease: the doctor will assess the risk-benefit of treatment with Adacolumn®.

Additionally you MUST ALWAYS:

- Monitor the patient's vital signs throughout the treatment, under nursing supervision, and in case of abnormalities under medical supervision.
- Work with peripheral veins whenever possible (when it is necessary to use a central venous catheter, the occurrence of general complications related to this type of procedure should be monitored).

Adacolumn® IFU Data Sheet
Cabriada JL, Doménech E, Gomollón F, González-Carro P, González-Lara V, Hinojosa J, et al. Consensus document on the use of granulocytoapheresis in patients with inflammatory bowel disease. Gastroenterol Hepatol. 2006; 29(2): 85-92
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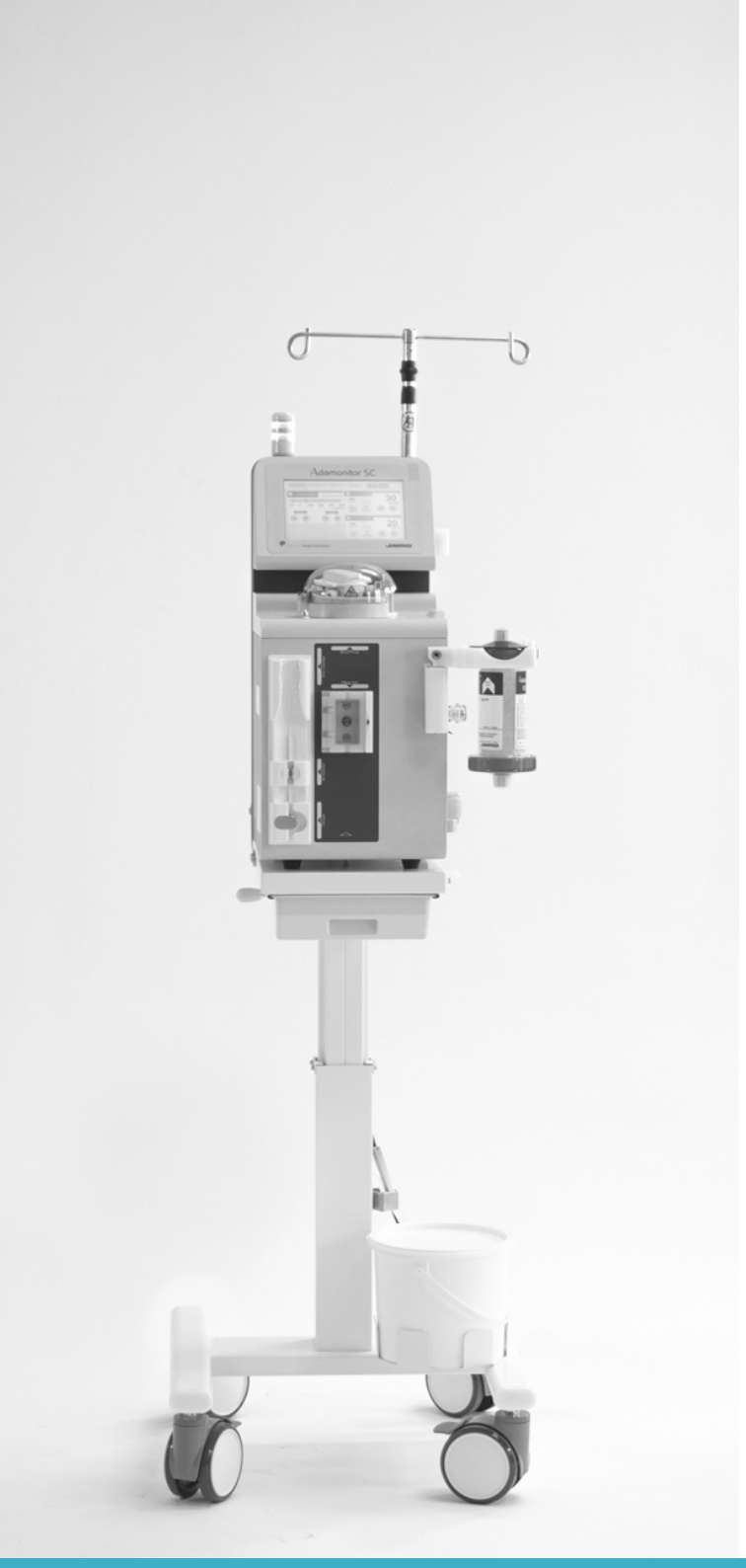


04

Equipment requirements for GMA procedure

4 EQUIPMENT REQUIREMENTS FOR GMA PROCEDURE

Material needed to administer apheresis

The following is needed to be able to apply the technique:

- **Adacolumn®:** sterile, single-use column for therapeutic apheresis by selective leukocyte adsorption. Contains 220 g of cellulose acetate beads bathed in physiological saline as the column adsorptive carriers. CE-certified Medical Device Directive 93/42/EEC by Notified Body TÜV SÜD Product Service GmbH (0123). N° G1 036676 0023.

- **Adamonitor®:** peristaltic pump that keeps the blood circulating inside the circuit. CE-certified Medical Device Directive 93/42/EEC by Notified Body TÜV SÜD Product Service GmbH (0123). N° G1 028492 0050.

- **Adastand**: structure that supports all the equipment necessary to carry out the technique.

- **Adacircuit:** Sterile, single-use tubing set consisting of an arterial and a venous line to be used for extracorporeal blood circulation during selective therapeutic apheresis of leukocytes. CE-certified Medical Device Directive 93/42/EEC by Notified Body TÜV SÜD Product Service GmbH (0123). N° G2 061967 0001.

- 20ml syringe: in order to be able to infuse heparin during the process, a specific syringe is supplied with the Adacolumn® and Adacircuit.

- 2 bottles of 1-litre normal saline:
  - 1 litre of normal saline.
  - 1 litre of heparinized saline with 4000 IU of Heparin.

- 2 needles, such as 18G.

- Heparin.

TABLE 7. PRELIMINARY CONSIDERATIONS AND RECOMMENDATIONS FOR THE PATIENT

Adequate information on the benefit and risk of the procedure.

In our environment they are usually performed in haematology or dialysis units by trained and specialised personnel. It can be performed at the day hospital. Adequate aseptic conditions must be maintained at all times.

The gastroenterologist responsible for treating IBD will supervise the process and assess the indication for a short course of oral steroids in a downward pattern for 4-6 weeks. If GMA is used after failure of immunosuppressive therapy, it is recommended to continue these drugs.

Preserve the patient's venous lines throughout the process:

- Perform exercises that strengthen the peripheral venous circulation in the upper extremities.
- Avoid unnecessary extractions (take advantage of the venous canalisation of each session).
- Recommend abundant liquid intake during the hours before treatment.
- Educate patient regarding preservation of access.

In case of fever due to a concomitant infectious process, it is advised to postpone the technique until it resolves.

In the case of treatment with angiotensin converting enzyme inhibitors (ACE inhibitors), the medication must be stopped at least 24 hours before the procedure (blocking ACE inhibitors can cause massive release of bradykinins triggering hypotension and shock).

It is unknown whether apheresis procedures are safe during pregnancy. The decision to use them must be on an individual basis.

RATIONAL USE OF GRANULOCYTE-MONOCYTE APHERESIS (GMA) IN INFLAMMATORY BOWEL DISEASE

TABLE 8. TECHNICAL ASPECTS OF THE PROCEDURE

Venous routes:	Assessment of peripheral venous access prior to the first session by qualified nursing staff. Antecubital catheterisation with a 17-gauge hemodialysis fistula needle (first choice) or with a 16-18-gauge venous catheter. The feedback allows canalisation with a smaller diameter, fistula type with side window. Proximal antecubital thick veins allow better flow; if access is not possible, it should be attempted progressively in more distal sections. If peripheral access is not possible, analyse individually the risk-benefit of using a central catheter for several weeks. If a line is lost during the session, the blood must be kept moving through the establishment of a closed circuit; this allows about 15 minutes to obtain access to a new line and restore the circuit to normal. It should be taken into account that the longer it is stopped, the greater is the probability of the circuit coagulating, which would force the session to be suspended.
Patient preparation:	Between 10 and 30 minutes before starting the session, an intravenous bolus of low molecular weight heparin (enoxaparin) will be injected with a dose adjusted to the patient's weight (e.g: Clexane® 0.8-1 mg/kg of weight). Alternatively, unfractionated heparin (sodium heparin) can be used in continuous perfusion for the duration of the apheresis. In hypercoagulable situations it may be necessary to adjust the dose to the therapeutic effect to avoid clotting of the circuit. Within 12 to 24 hours after the procedure, the patient should avoid activities with a high risk of trauma.

TABLE 8. TECHNICAL ASPECTS OF THE PROCEDURE (CONTINUED)

Safety:	Avoid the possibility of infection. Compliance with standardised bloodline care procedures. Serious adverse effects of the procedure are rare. However, it is advisable to have a supply of intravenous medication: paracetamol, adrenaline, antihistamines, hydrocortisone; needles and syringes; saline and ringer.
Monitoring:	Hemodynamic monitoring (heart rate, blood pressure, T°) at baseline and during the procedure especially in: elderly patients, cardiovascular disease, kidney failure, liver failure or treatment with ACE inhibitors. Review the clinical situation of the disease, adjust the concomitant medication and assess the performance of a rectosigmoidoscopy before starting the technique. It useful to have an analysis, including coagulation parameters, in a baseline form and after the 3rd apheresis session, as well as at the end of the cycle. Assess the efficacy of granulocyte-monocyte apheresis (GMA) after steroid withdrawal and systematically record clinical information.

05

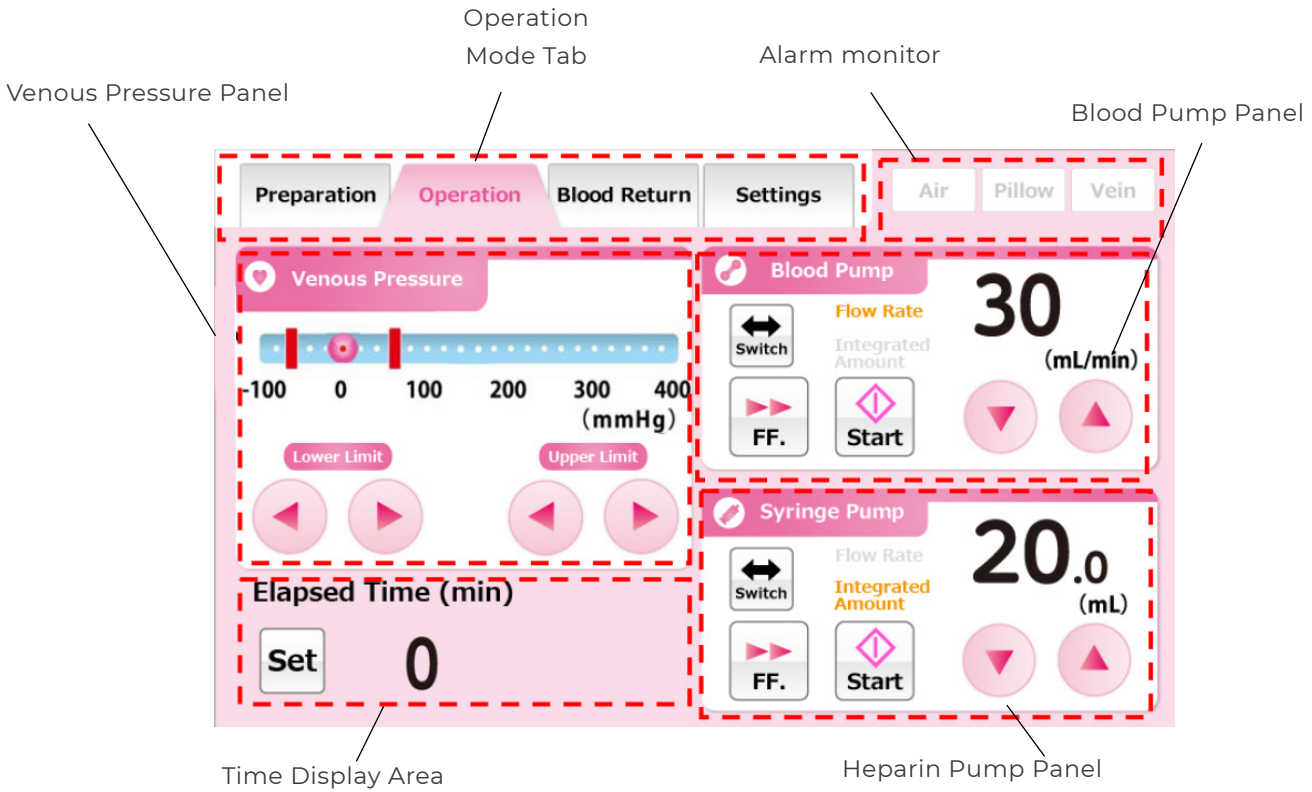
Adamonitor® SC main screen

5 MAIN SCREEN

The main screen is used to select the different working modes (Preparation, Operation, Blood Return) and set the device.

The parts that can be adjusted are:

- Venous Pressure Sensor
- Blood Pump Panel
- Heparin Pump Panel
- Time Display Area

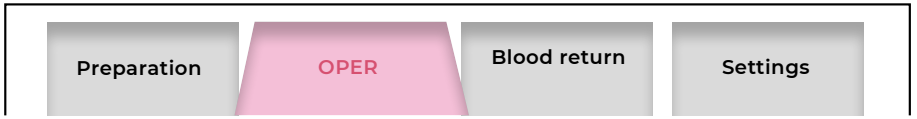


5.1 WORKING MODALITIES

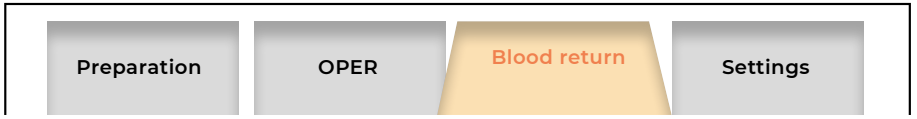
There are 4 working modalities:

- **Preparation mode:** This option is activated for cleaning and priming the blood circuit with normal saline solution.

- **Operation mode:** Modality used during the therapeutic apheresis process.



- **Blood return mode:** Mode used to return the blood remaining in the Adacircuit and Adacolumn® to the patient after completing the apheresis procedure.



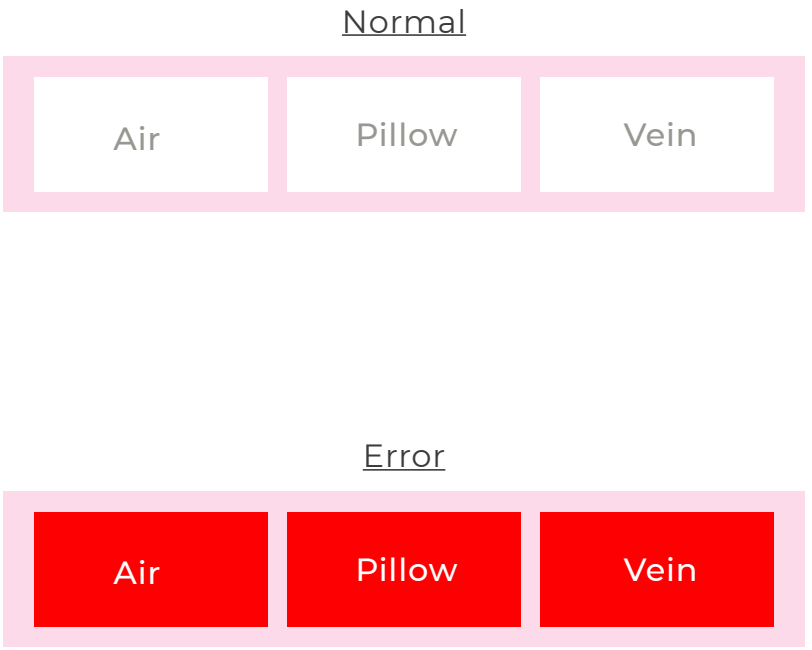
- **Settings mode:** Tab that allows you to make adjustments on the device: normal venous pressure range, blood pump flow rate, heparin pump flow rate, etc.

5.2 ALARM TYPES

- **Aire:** The air alarm indicates the presence of air bubbles in the blood outlet line. In addition to the activation of the alarm signal, the Adamonitor® also activates the locking clamp to prevent air from entering the patient.

- **Pillow unit**: Blood pressure monitoring using the pillow unit is intended to increase the safety of the blood supply line. Usually, the blood pressure monitor (pillow unit) detects an occlusion at the blood supply line.

- **Vein:** Venous pressure monitoring allows us to increase the safety of the venous line or blood outlet. Usually, the loss of venous pressure is caused by a broken connection in the region of the blood outlet line. High venous pressure can be caused by a blockage that prevents venous access to the outlet line.



What to do if...

The alarm “PILLOW UNIT” is activated on the Adamonitor® during the procedure:

This alarm indicates insufficient blood flow from the patient.

Confirm that the IV access needle clamps and blood supply line (clamp 1) are open. Check that the patient's arm is straight and has not moved.

Give the patient an anti-stress ball to squeeze lightly.

Apply a tourniquet with light pressure.

Try a slower rate (25 ml/min and gradually increase over 10 min to 30 ml/min).

Try to readjust the access needle (attach a small syringe to check blood flow).

Reposition the access needle (change of location).

5.3 TROUBLESHOOTING GUIDE

What to do if...

The alarm "VEIN" is activated on the Adamonitor® during the procedure:

This alarm indicates that the venous pressure exceeds the upper or lower limits set by the user.

Confirm that the blood return line (clamp 2) and return needle (*if used*) are open. Check that the patient's arm is straight and has not moved.

Examine the tissue at the catheterisation site for weakening.

Purge the return cannula with heparin or saline.

Try to reposition the cannula (pull the tip of the cannula back slightly; it may be touching a valve).

Reposition the cannula (change of location).

What to do if...

The "AIR" alarm is activated on the Adamonitor® during the procedure:

This alarm indicates the presence of air in the blood return line or that the blood outlet line is not properly attached to the air bubble detector.

Confirm that the blood return line is securely attached to the air bubble detector.

If air is present *(it will be next to the bubble detector)* close clamp 3, remove the blood return line from the detector and gently tap the air into the injection port where it can be removed using a syringe with a needle. Check if it is necessary to adjust the fluid level in the air vent.

If this alarm is goes off again, you have forgotten to activate the heparin infusion. (*blood may have clotted in the system*).

5.3 TROUBLESHOOTING GUIDE

Weakening of the catheterisation point:

In case of weakening of one of the catheterisation points, the affected point shall be replaced by another one as soon as possible. If this cannot be done in less than a minute, you must take steps to prevent the blood from clotting within the system.

Connect the blood supply line to the normal saline bag and run the system until the saline flushes the blood out of the inlet line. Connect the blood supply and blood outlet lines together with a "male-male" connector and press **“START”** to continue circulating the system. After one minute, stop the heparin infusion. Purge the unaffected catheterisation site with heparin or saline.

You will have 5 minutes to re-establish intravenous access. If successful, reconnect the supply and return lines and resume treatment and heparin infusion. Do not forget to add any minutes that were lost at the end of the procedure. If unsuccessful, connect the blood return line to the catheterisation point still in use, open the clamps and roller clamp, select the “Blood return” tab, press **“START”** and invert the column to begin blood return to the patient.

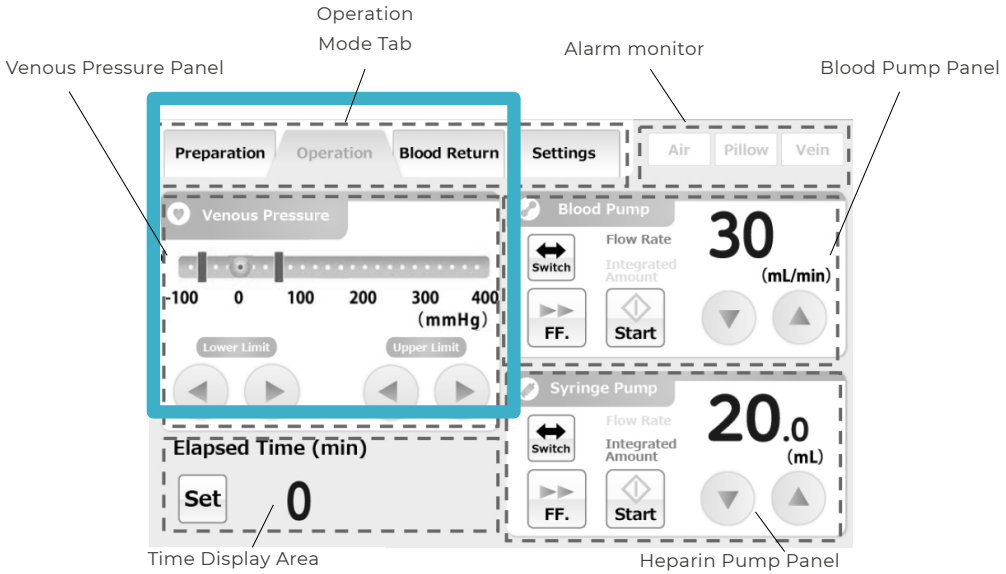
Normally, if the patient has been treated for more than 30 minutes, it can be considered a complete treatment.

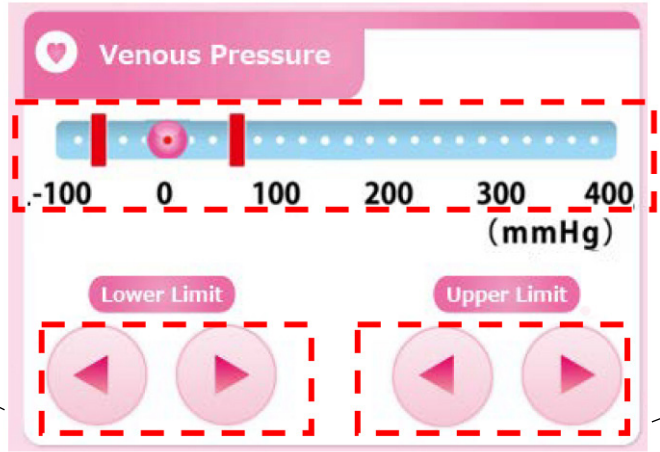
Intolerance/adverse effects on the patient:

Normally, in the above cases, it is best to perform a normal blood return if the procedure cannot be continued, **except when there is a suspected reaction to heparin,** in which case treatment should be discontinued without blood return.

5.4 VENOUS PRESSURE

Panel that gives the option of monitoring Venous Pressure and changing the normal range of Venous Pressure.





Venous pressure sensor

Button to change the lower limit of the venous pressure

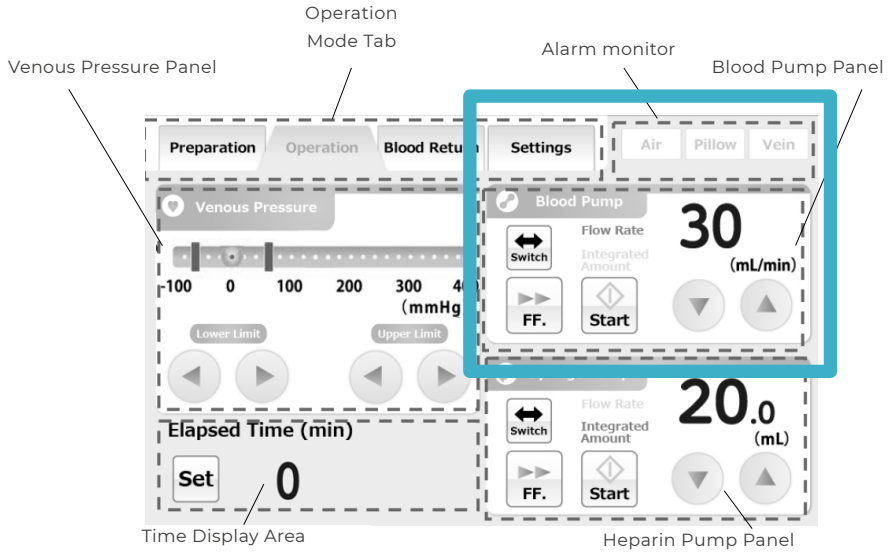
Button to change the upper limit of the venous pressure

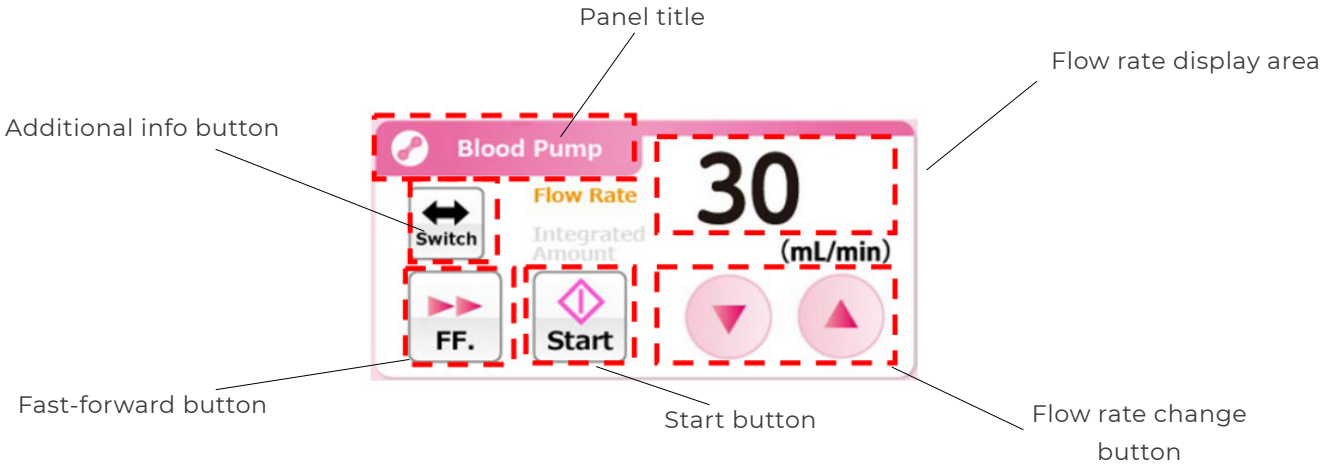
5.5 BLOOD PUMP PANEL

Panel used to display and control the flow rate at which we are operating.

Notes:

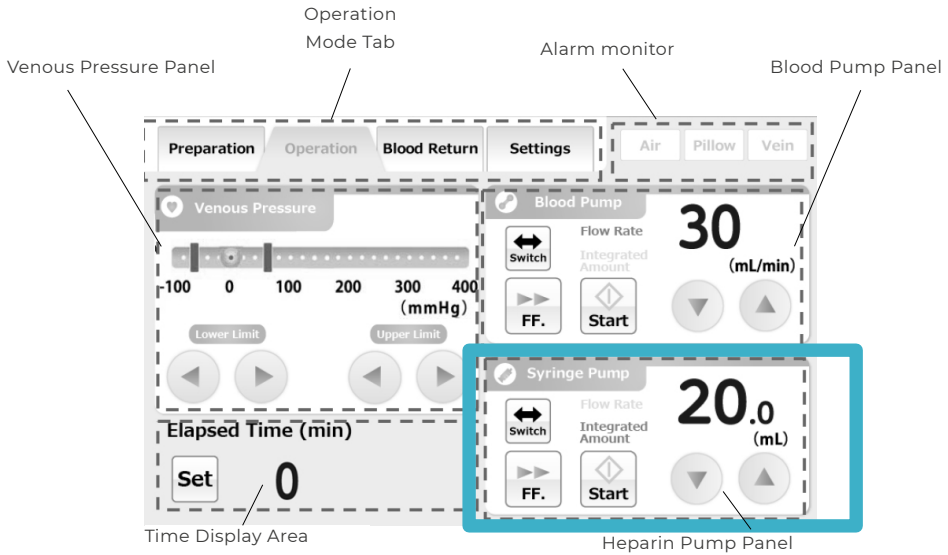
- The fast forward button is enabled only in Preparation mode.
- The flow rate can be changed when the blood pump is running.
- Flow speed: min 10 ml/min - max 50 ml/min
- In fast forward, the flow speed can reach max 150 ml/min.
- The switch button shows you the volume of blood processed.





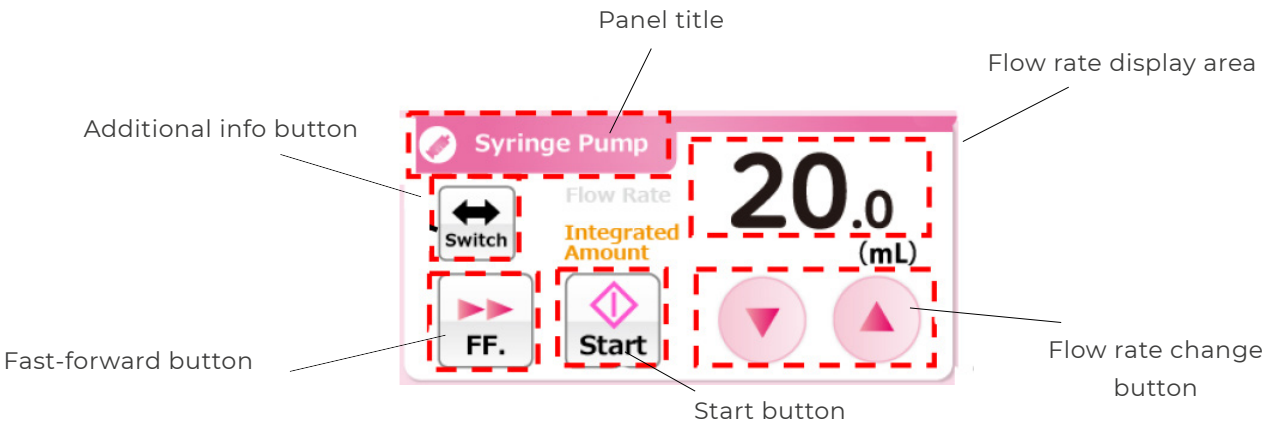
5.6 HEPARIN PUMP PANEL

Panel allowing control of the heparin pump and the amount of fluid administered.



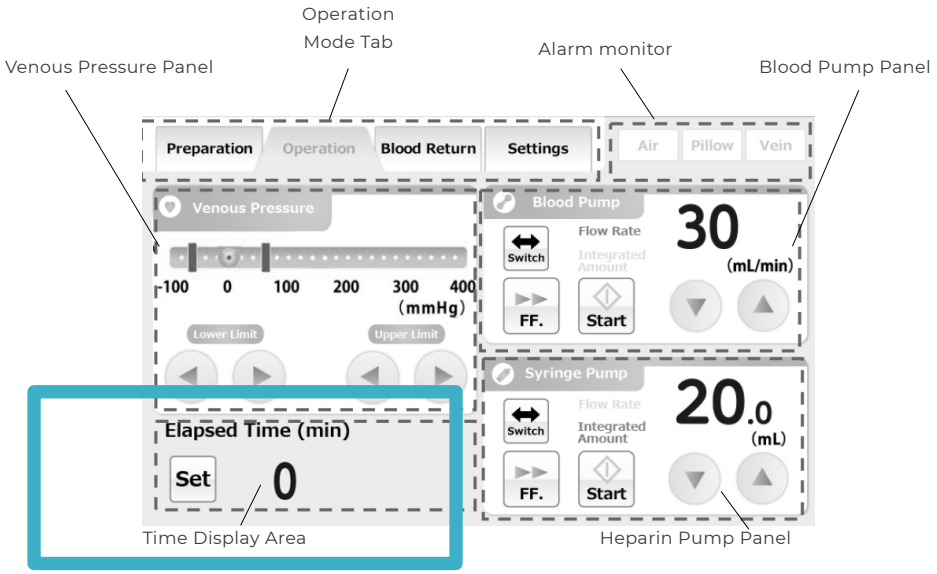
Notes:

- The flow rate can be changed when the heparin pump is running.
- The fast-forward flow rate cannot be changed.
- Flow speed: min 1 ml/h – max 20 ml/h
- The switch button shows you the total amount of heparin processed.



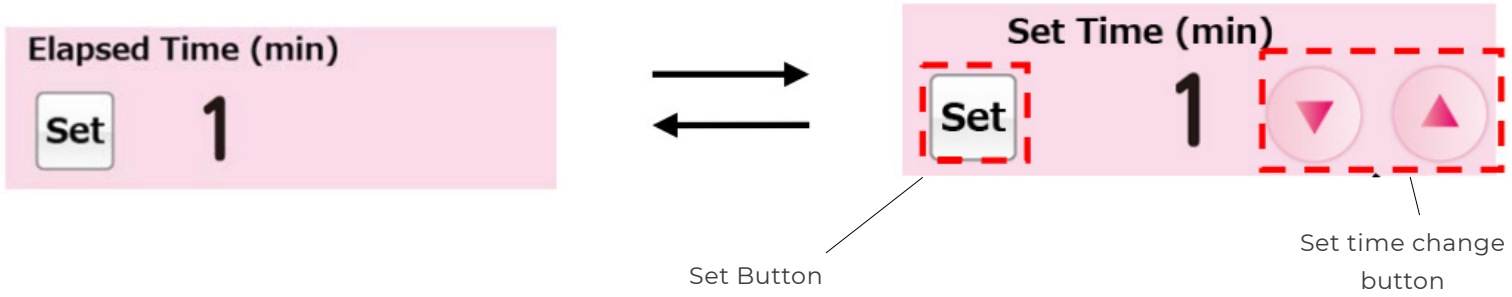
5.7 TIME DISPLAY AREA

The circulation time can be displayed and changed in this area.



Notes:

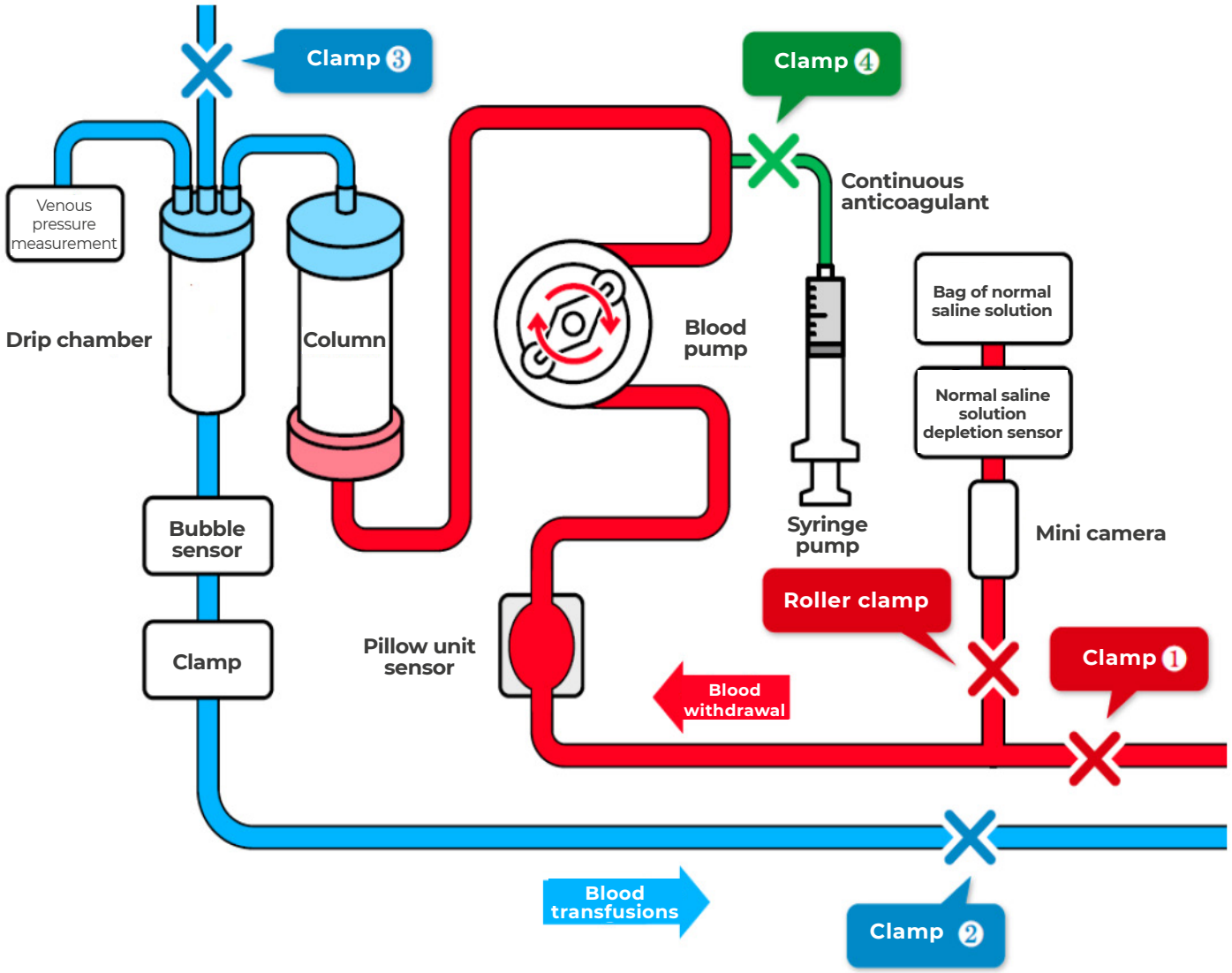
- The set time can be adjusted to a maximum of 180 minutes.
- The set time is reflected in real time on the system each time the button is pressed to change the set time.



06

Operational method

CIRCUIT DIAGRAM



6.1 PREPARATION

1. **Check expiration dates of Adacolumn® and Adacircuit**.
2. Place **Adastand and Adamonitor® SC** in the correct position and carry out a visual inspection.
3. Connect the **Adamonitor® SC** to the power supply.
4. Switch on the **Adamonitor® SC** and let it perform the self-test.
5. Prepare the **20 ml syringe of the Adacircuit** with heparin according to the protocol (explained later).
6. Add 4,000 units of **heparin** to a **1 litre bag of normal saline.**

6.2 **ASSEMBLY (I)**

1. Hang a **1 litre bag of normal saline solution** on the **Adastand**. This will be used to prime the Adacircuit and for blood return. Approximately 500 ml for priming and 500 ml for return.

2. Hang a **1 litre bag of heparinised saline** on the **Adastand** (heparin 4000 UI in 1 litre normal saline). This will be used to clean the Adacircuit system after priming.

3. Open the **Adacircuit**. It consists of 4 parts:

    - **The blood supply** line (red or arterial).
    - **The blood return** line (blue or venous).
    - The sterile waste bag.
    - **A 20 ml syringe** (for heparin infusion).

4. Take the **20 ml syringe**. Add the **heparin** dose with normal saline to the syringe.***

***Example:** If we decide to administer 4,000 IU/ml during the process, we would add to the 20ml syringe:

- **Heparin (1,000 UI/ml): 4ml heparin + 16ml saline solution.**
- **Heparin (4,000 UI/ml): 1ml heparin + 19ml saline solution.**

6.2 ASSEMBLY (II)

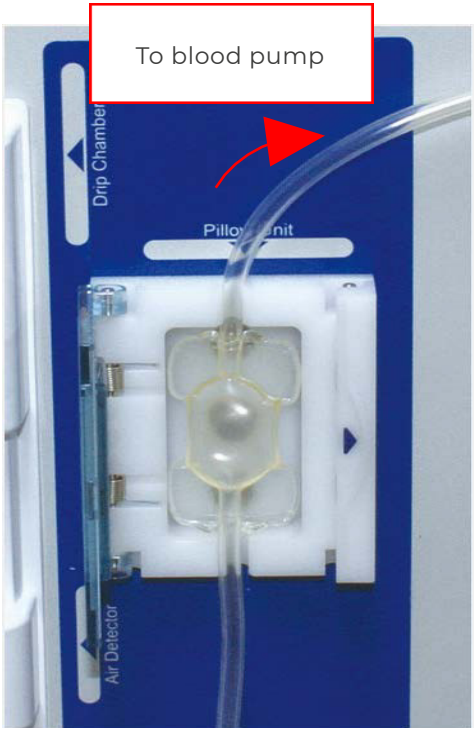
5. Take the **blood supply line (Red)**. Ensure that both detachable intravenous tips are firmly connected (if necessary). Close all **clamps** on the circuit.

6. Connect the **additional infusion line (with drip chamber)** to the 1 litre **bag of normal saline solution.**

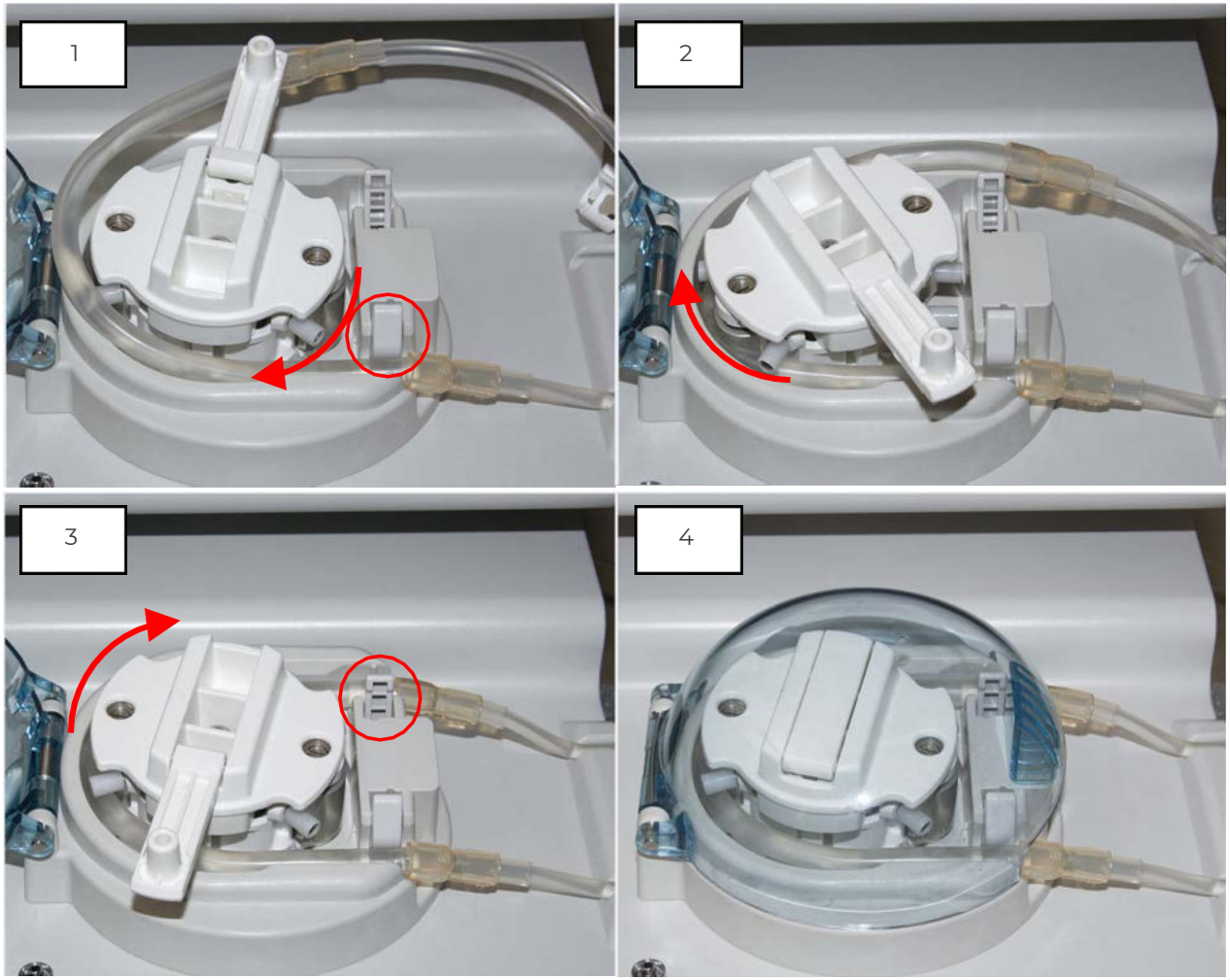
7. Support the **blood supply line** by hanging it on the **Adastand support.**

8. Locate the **"pillow section"** and place it inside the pillow sensor casing, making sure the **flow** goes up through the sensor.

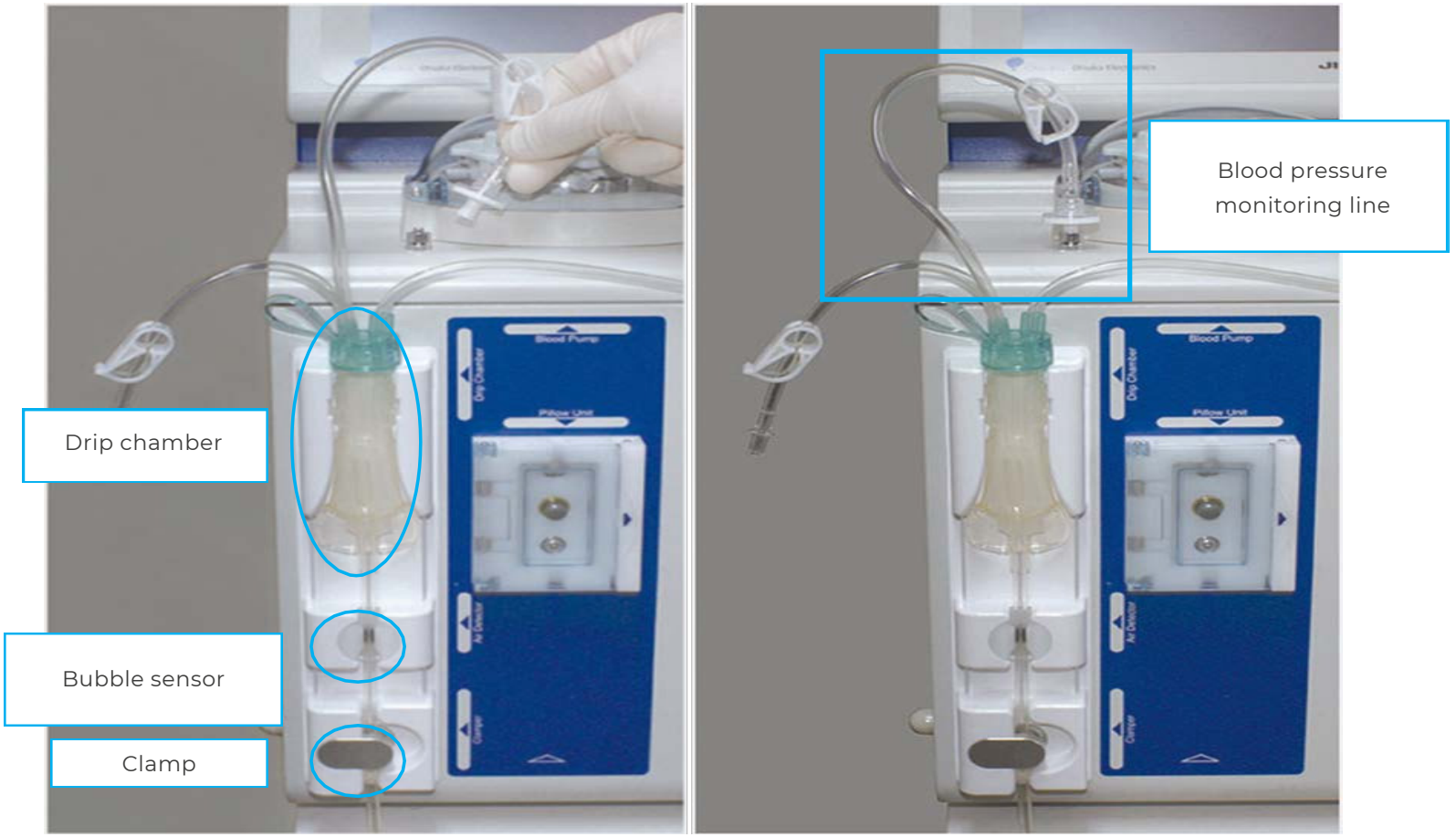
9. Open the pump cover. Place the thick part of the arterial line through the pump rollers. Close the pump cover.



10. Take **the blood return line (blue)** and insert the **drip chamber** into the Adamonitor® SC drip chamber holder.



11. Insert the line through the **air bubble detector.**



12. Connect **the venous pressure measurement line to the venous pressure monitor.**

13. Remove the **connector** from the end of the blood outlet line, connect the line to the **waste bag**. Keep the connector safe for later use. Place the waste bag in the **bucket** and secure the line in the holder.

14. Remove **Adacolumn®** from its packaging and place it in the Adacolumn® holder of the Adamonitor®. Red side up.

15. Remove the **tab from the red** Adacolumn® connector and connect it to the red side of the Adacolumn®.

16. **Replace the Adacolumn® in the holder, blue side up**. Remove the blue connector tab and connect it to the blue side of the Adacolumn®.

17. Open the roller clamp at the additional infusion line. Invert the **drip chamber**. Open **clamp 1** at the blood supply line and allow the drip chamber to fill to 75%. Then close clamp 1 and place the drip chamber correctly. Now open clamp 1 until saline drips from the blood supply line and then close clamp 1.

18. Connect the **blood supply line to the 1 litre bag of heparinised saline**.

19. Insert the **additional infusion line into the fluid interruption sensor.**

6.3 PRIMING

1. To initiate priming, press and hold the **start button** until the blood pump is activated.

2. Press and hold the **FF button {quick flow}** until the pump accelerates.

3. Allow the saline solution to fill the Adacolumn® and then shake the column until most of the air has been removed.

4. When air has been removed from the column, stop the pump, **press and hold STOP** until the pump stops. Close **clamp 2** on the blood outlet line.

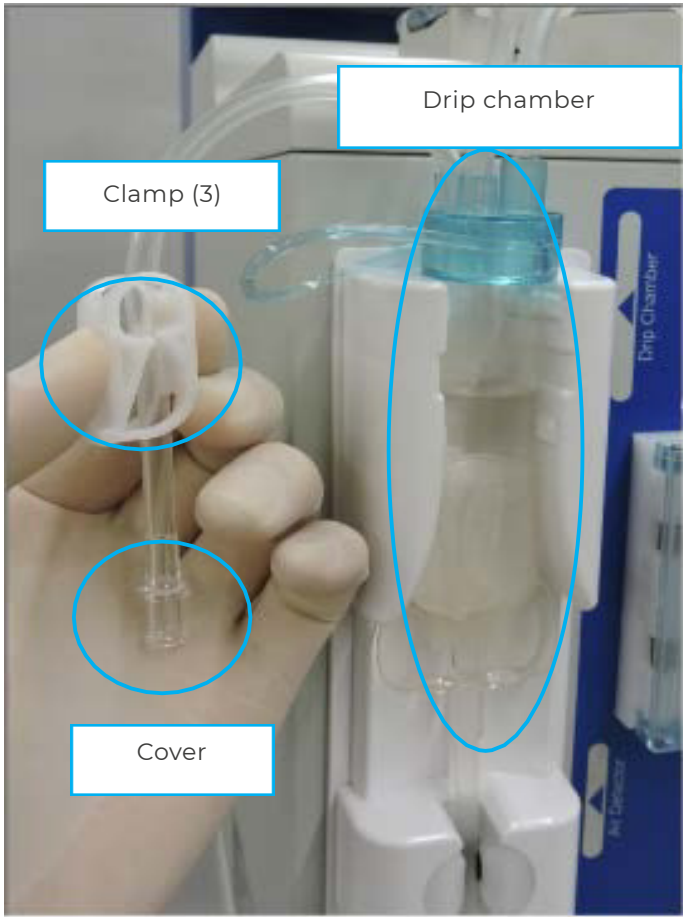
5. To fill the **drip chamber:**

    - *Remove the **cap from the air adjustment** line and confirm that **clamp 3** is open.*

    - *Press **START** until the pump starts; allow the drip chamber to fill to 75% and then press **STOP.***

    - *Close **clamp 3** on the air adjustment line and replace the **cover.***

6. Open **clamp 2** on the blood outlet line, **press START** to activate the pump and then **press FF {quick flow}**. Once all the air has been removed from the blood outlet line, press **STOP** and close the **roller clamp**.



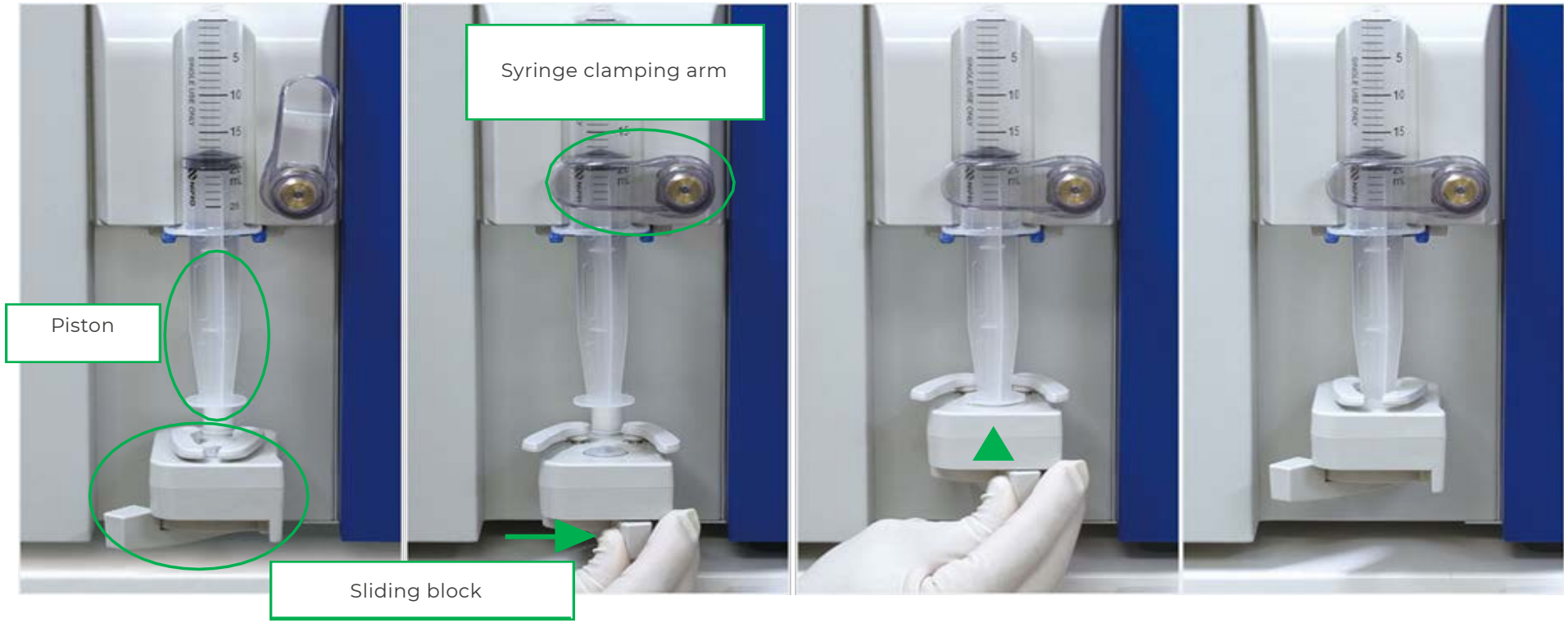
6.4 SYSTEM HEPARINISATION (I)

1. Open **clamp 1 of the blood supply line.**

2. **Press START and then FF** - wait 2 minutes for the heparinised saline solution to flow through the system.

3. After these 2 minutes, **press STOP** and close **clamp 2** on the blood outlet line

4. Fill the **heparin infusion line**: remove the **cap** from the heparin line and then **press START.** When the saline solution drips from the heparin line, **press STOP** to stop the pump. Attach the prepared **heparin syringe** and close the heparin line **clamp**. Place the syringe in the syringe pump.



6.4 SYSTEM HEPARINISATION (II)

5. Open **clamp 2 on the blood outlet line.**

6. **Press START and then FF.**

7. Move the column and rotate it punctually to ensure that the heparinised saline solution is impregnated throughout the column.

8. Check that the Adacolumn® has removed the air, if necessary {as described above}.

9. When there are about 50 ml of heparinised saline left, **press STOP.**

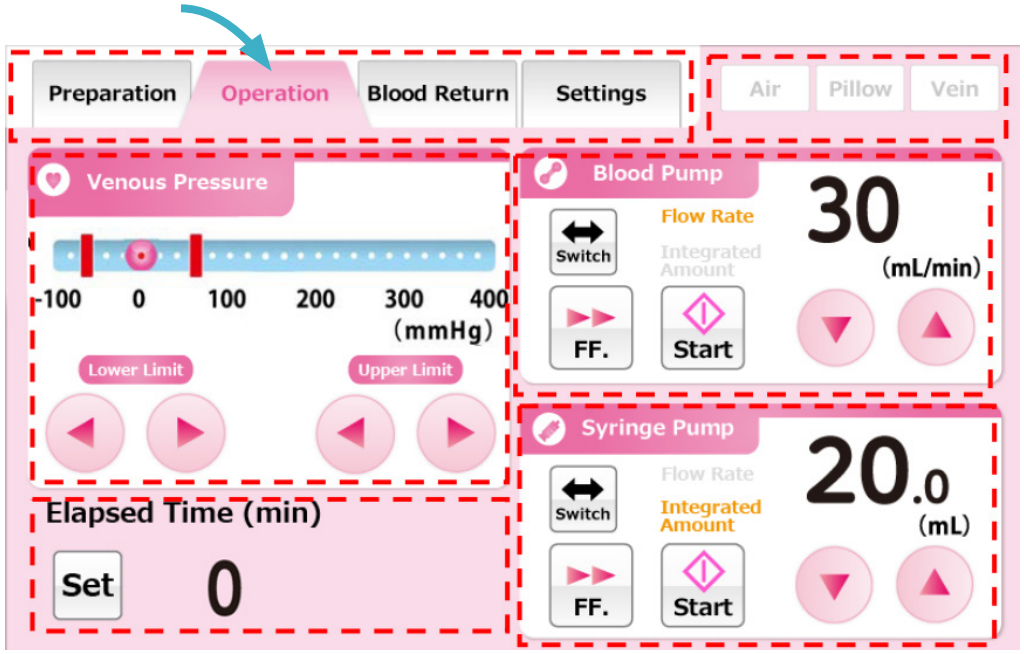
6.5 LEAK TESTING

Leak testing on the Adamonitor® SC is fully automated. Apheresis cannot be started (operation mode) until a successful leak test has been performed.

1. Press and **hold "Leak Test",** the device will start the leak test and will indicate whether the system is leaking or not after about 20 seconds.

2. Close **clamps 1, 2 and the waste bag clamp.**

3. Then **click on the "OPER" tab** to start treatment. With these checks the device is now ready to start treatment.



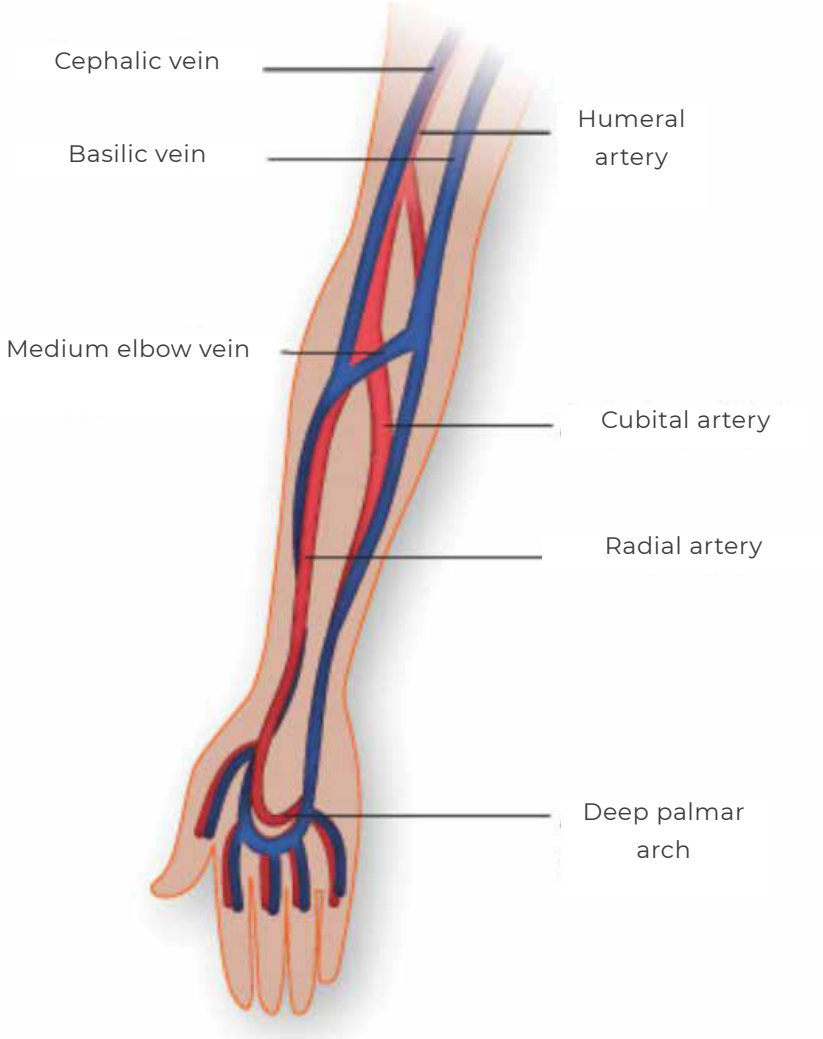
6.6 VENOUS ACCESS

The best sites to establish venous access are the **antecubital veins.**

Blood should be drawn from one side and returned to the opposite limb. Use the **side with the best vein for blood withdrawal** and thus minimise blood flow problems.

Use the **18G needle** for optimal blood withdrawal and an 18G or 20G IV cannula for blood return. If preferred, the cannulae can be used for both blood withdrawal and return.

First insert the IV cannula for venous return and then connect the blood outlet line.

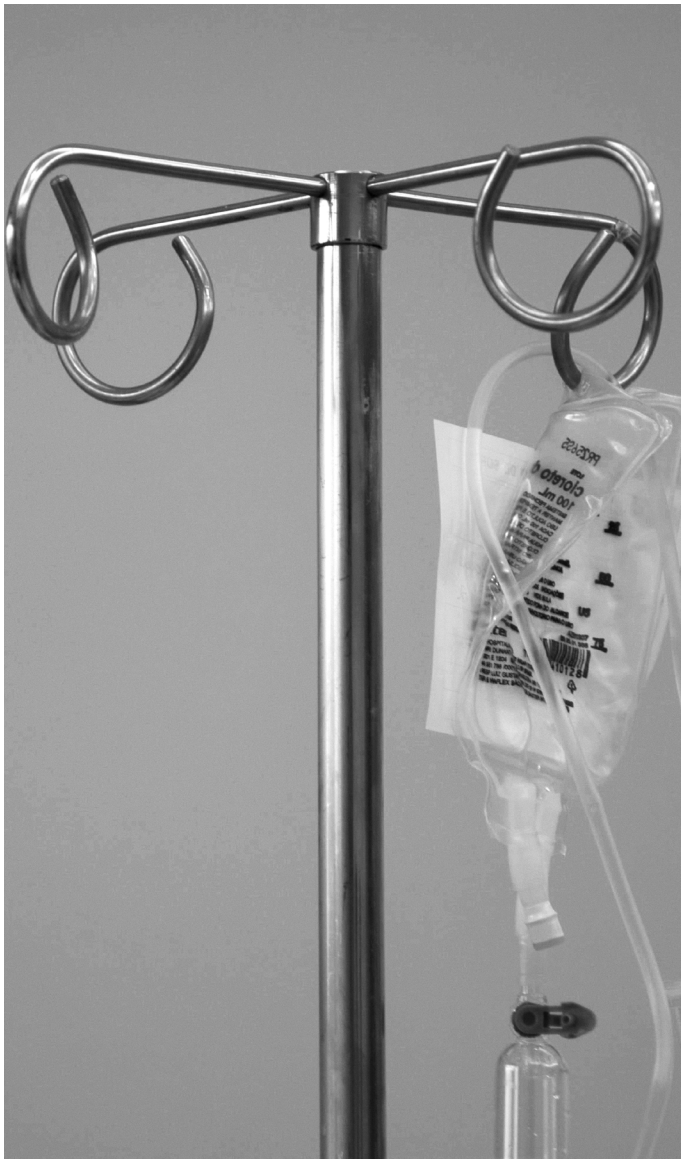


6.7 CANNULATION TIPS (I)

- Assess patients veins prior to treatment.
- Advise the patient to undertake arm exercises on a daily basis if the veins are difficult to find (using weights or grip strengthener).
- The patient should be well hydrated on treatment day.
- Advise the patient to wear short-sleeved clothing that does not excessively constrict the arms on the day of treatment.
- The patient should not be cold: applying local heat helps to dilate the veins.
- Do not over-tighten the tourniquet.
- Leave the best vein for the blood access site.

6.7 CANNULATION TIPS (II)

- If using an IV cannula for venous return, insert it first.
- When examining catheterisation sites, always identify another site as an alternative.
- Have a working knowledge of the anatomy of the forearm veins.
- Note the catheterisation site used and note the methods used to obtain access.
- Tell the patient how blood flow can be improved (stretching the arms, using a stress ball, etc.).



6.8 TREATMENT (I)

The procedure for Adacolumn® treatment is:

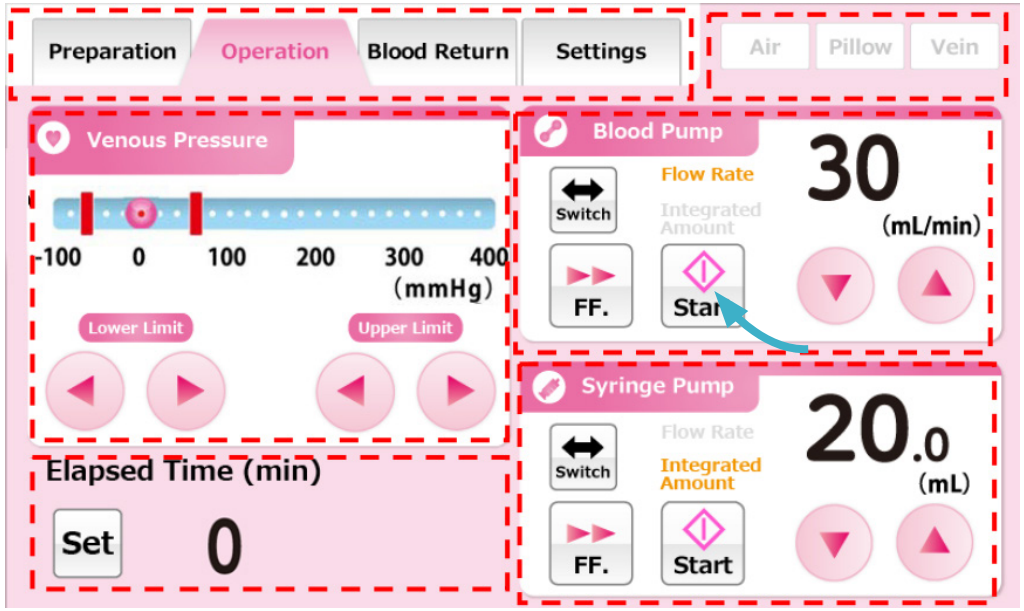
1. Disconnect the **blood return line** from the waste fluid bag and connect it to the **return needle/cannula.**

2. As soon as possible after insertion of the access needle, disconnect the **supply line from the bag of heparinised saline solution** and connect it to the **access needle.**

3. Open clamps **1, 2 and the needle access** (if available). Then press **START** on the blood pump window to start the treatment.

4. The heparin pump will automatically start at the rate set in the heparin pump window.

5. Check that the **blood** flows freely along the blood supply line and that the venous pressure remains within normal limits.



6. If necessary to maintain the flow, a stress ball can be used to stimulate blood flow and/or apply a tourniquet with light pressure.

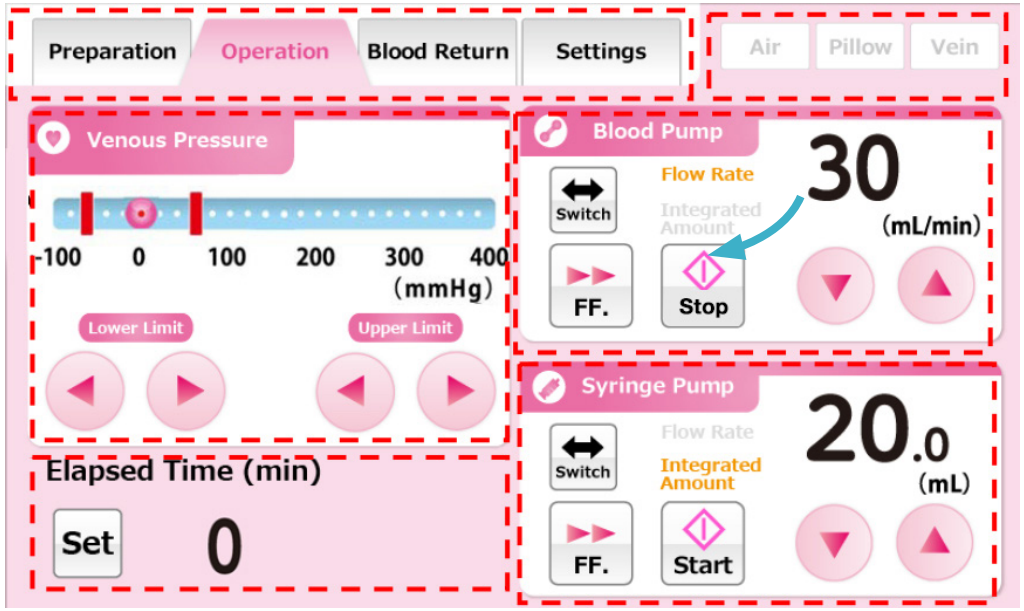
7. If necessary, use the **SWITCH** button to display the **flow** of the treated volume.

8. If necessary, use the **SWITCH** button on the syringe pump menu to change the **flow** display to volume infused

6.9 BLOOD RETURN (I)

A continuous low-volume alarm is activated once the set processing time has elapsed. The pump will continue to operate.

1. Press **STOP** to stop the pump, remove the tourniquet and stress ball (if used), and open the **roller clamp** to allow the normal saline solution to remove blood from the blood supply line (this takes about 15 seconds). When the line becomes "Pink" close **clamp 1** and the **IV needle clamp** (if used).



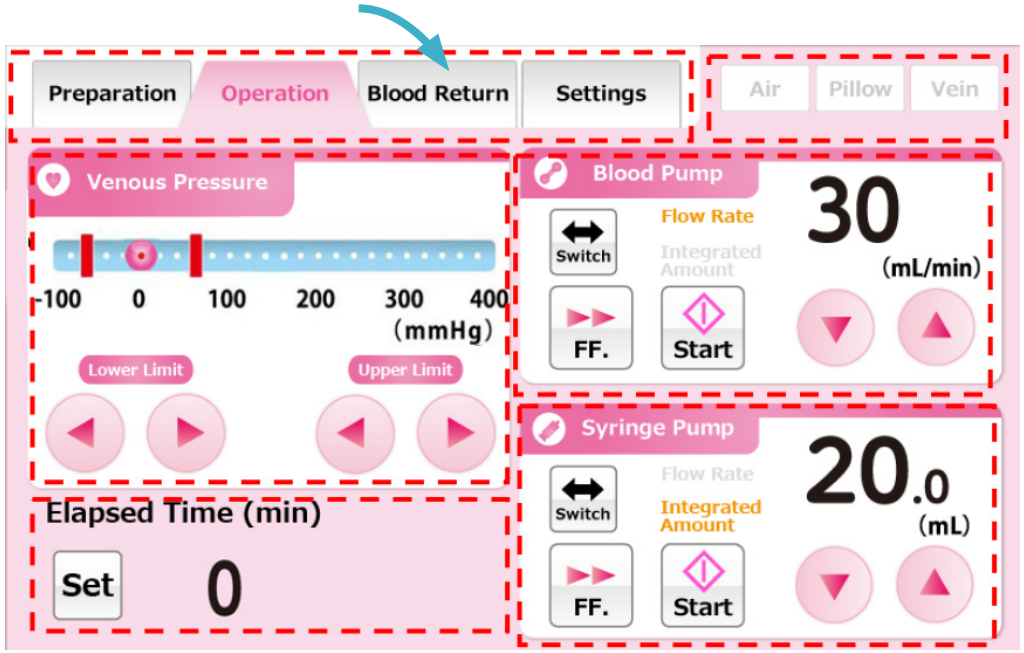
6.9 BLOOD RETURN (II)

2. Press the **"Blood Return" tab** and press **START** to begin returning blood to the patient. Make sure you have enough saline solution to complete the blood return (about 500 ml).

3. Invert the **Adacolumn®** in the Adastand to help the complete return of blood, (red side up).

4. Remove the **IV access needle** from the patient. Connect the **blood supply line** to the connector to the saline bag hanging from the holder. The blood return procedure usually takes about 10 minutes; stop the blood return when the saline bag runs out or the return fluid turns a very light pink colour, (press **STOP**). Close **clamp 2** and then remove the **final IV access device** from the patient.

5. The **Adamonitor®** can now be switched off



6.10 ADACOLUMN® AND ADACIRCUIT DISPOSAL

1. Disconnect and safely dispose of both devices.

2. Use the lock to connect the **blood supply and outlet** lines.

3. Disconnect the **extra infusion line from the IV tip** and connect it to the venous pressure monitor line.

4. Close **clamp 4** and remove the **syringe** from the infusion pump. Tie a knot in the **heparin infusion line.** Adacolumn® & Adacircuit may still contain patient blood but now the Adacircuit is sealed and the risk of leakage is minimal.

5. Dispose of the Adacolumn® & Adacircuit as infectious waste according to the regulations in force in the country of use and in accordance with the facility's standard procedures. Treat the plastic IV tips as sharp objects when disposing of them.

ADAMONITOR® ERROR MESSAGES

Adacolumn®

All error messages that may appear on the Adamonitor® are displayed here.

MONITOR INDICATOR	DETECTED ERROR	SOLUTION
C1	Clamp	Critical error
C2	Clamp	Critical error
C3	Pump cover	Close the pump cover
C4	Pump	Critical error
C5	Battery	Low battery charge
C6	Abnormal interruption in the previous session	Press the Reset button
C7	Other equipment failure	Critical error

For codes C1, C2, C4 and C7 it is recommended to turn the device off and on again to try to reset it. If the error continues, please contact us for technical support. Have the serial number of the Adamonitor® on hand.

- From Spain: +34 900 180 135
- Outside of Spain: +800 222 444 70
- Email: *customerservice@adacyte.com*

Our technical service will check the device annually. In the meantime, any complaint or incident occurring with the device must be reported immediately to *vigilance@adacyte.com* within 24 hours.

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Thank you very much

EN-ADA-1120042