

Claims

1. An extracorporeal blood treatment system (50) for treating a subject suffering from cancer, the system comprising:
 - 5 an extracorporeal blood circuit (52a, 52b);
 - a dialysate fluid circuit (54a, 54b);
 - said extracorporeal blood circuit (52a, 52b) and dialysate fluid circuit (54a, 54b) being divided by a membrane (59) of a filtration unit (58);
 - at least one blood pump (60) for controlling the flow of blood through the blood circuit (52a, 52b);
 - 10 at least one dialysate fluid pump (62, 68) for controlling the flow of dialysate fluid through the dialysate fluid circuit (54a, 54b);
 - optionally one or more infusion lines (66, 80, 81, 82), each infusion line being connected to the extracorporeal blood circuit (52a, 52b) or adapted for being directly connected to the vascular system of the subject to be treated, each infusion line comprising an infusion pump;
 - 15 a system computing unit (64) operatively connected to the blood pump (60) and the dialysate fluid pump (62, 68) and optionally to the one or more infusion pumps of the one or more infusion lines (66, 80, 81, 82), said system computing unit having a user interface including an input means and a display means; wherein
 - the system computing unit (64) is adapted for receiving a desired blood concentration value GLN_b of glutamine (901) within the range of 0.1 and 0.5 mM;
 - the system computing unit (64) is adapted for receiving a desired blood concentration value $GLUCOSE_b$ of glucose (903) within the range of 2 to 4 mM;
 - 25 the system computing unit (64) is adapted for receiving a desired blood concentration value $KETONE_b$ of a ketone body, such as acetoacetate, beta-hydroxybutyrate or pharmaceutically acceptable derivatives, esters and salts thereof (905) within the range of 1 – 15 mM;
 - the system computing unit (64) is adapted for receiving a concentration value GLN_p representing the concentration of glutamine or pharmaceutically acceptable glutamine-containing compounds in fresh dialysate fluid (902);
 - 30 the system computing unit (64) is adapted for receiving a concentration value $GLUCOSE_p$ representing the concentration of glucose in fresh dialysate fluid (904);
 - optionally, the system computing unit (64) is adapted for receiving a concentration value $KETONE_p$, representing the concentration of a ketone body, such as acetoacetate, beta-hydroxybutyrate or pharmaceutically acceptable derivatives, esters and salts thereof in fresh dialysate fluid (907);
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- optionally, the system computing unit (64) is adapted for receiving a concentration value $KETONE_i$ representing the concentration of a ketone body such as acetoacetate, beta-hydroxybutyrate or pharmaceutically acceptable derivatives, esters and salts thereof in an infusion liquid to be infused into the extracorporeal blood line (52b) or directly into the vascular system of said subject to be treated, through one of said one or more infusion lines (66, 80, 81, 82) (906);
- the system computing unit (64) is adapted for receiving an actual concentration value GLN_a of glutamine in blood from said treated subject (909) and receiving an actual concentration value $GLUCOSE_a$ of glucose in blood from said treated subject (910) and receiving an actual concentration value $KETONE_a$ of a ketone body such as acetoacetate and/or beta-hydroxybutyrate (911);
- the system computing unit (64) being adapted for controlling said blood pump (60) and said dialysate fluid pump (62, 68) in such a way that the actual blood concentration value GLN_a of glutamine is driven towards or below GLN_b (912) and the actual blood concentration value $GLUCOSE_a$ of glucose is driven towards or below $GLUCOSE_b$ (914);
- and
- if the system (50) comprises one or more of said infusion lines (66, 80, 81, 82) and in case one of said infusion lines (66, 80, 81, 82) is adapted for infusing said infusion liquid into the extracorporeal blood line (52b) or directly into the vascular system of said subject to be treated, the system computing unit (64) is adapted for controlling said infusion pump of said infusion line in such a way that the actual blood concentration value $KETONE_a$ is driven towards $KETONE_b$ (920); or alternatively
- if the system (50) does not comprise such an infusion line (66, 80, 81, 82), the system computing unit (64) is adapted for comparing $KETONE_a$ and $KETONE_b$, and if $KETONE_a < KETONE_b$, displaying a message on said display informing that the treated subject should consume a further amount of ketone bodies or medium chain triglycerides.
2. An extracorporeal blood treatment system (50) according to claim 1, wherein the system (50) comprises one or more of said infusion lines (66, 80, 81, 82), and the system computing unit (64) is adapted for receiving a concentration value $KETONE_i$ representing the concentration of a ketone body such as acetoacetate, beta-hydroxybutyrate or pharmaceutically acceptable derivatives, esters and salts thereof in an infusion liquid to be infused into the extracorporeal blood line (52b) or directly into

- the vascular system of the subject to be treated, through one of said one or more infusion lines (66, 80, 81, 82) (906), and
the system computing unit (64) is adapted for controlling said infusion pump of said infusion line in such a way that the actual blood concentration value KETONE_a is driven
5 towards KETONE_b (920).
3. An extracorporeal blood treatment system (50) according to claim 2, wherein the system computing unit (64) is adapted for monitoring GLN_a and initiating infusion of a composition containing glutamine or pharmaceutically acceptable glutamine-containing compounds if GLN_a is lower than GLN_b (916) by starting a relevant infusion pump in
10 one of the one or more infusion lines (66, 80, 81, 82), and maintaining said infusion until GLN_a is equal to GLN_b.
4. An extracorporeal blood treatment system (50) according to any one of claims 2 to 3, wherein the system computing unit (64) is adapted for monitoring GLUCOSE_a, and initiating infusion of a composition containing glucose if GLUCOSE_a is lower than GLUCOSE_b (918) by starting a relevant infusion pump in one of the one or more infusion lines (66, 80, 81, 82), and maintaining said infusion until GLUCOSE_a is equal to GLUCOSE_b (918).
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5. A system according to any preceding claim wherein the filtration membrane has a molecular weight cut off (MWCO) of less than 60kDa.
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6. A system according to claim 5 wherein the filtration membrane has a MWCO of less than about 50kDa or less than about 40 kDa (such as less than 30 kDa, less than 10 kDa, less than 5 kDa or less than 2 kDa).
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7. A system according to any preceding claim wherein the blood circuit comprises a thermal management system for heating or cooling blood in the blood line during use.
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8. A system according to claim 7 wherein the thermal management system is controllable to regulate the temperature of blood in the blood circuit to a temperature between 20°C and 43°C.
9. A system according to any preceding claim, further comprising on or more sensors (S, 90, 91, 92, 93) for the detection of analytes selected from the group glucose, glutamine, and ketone bodies, the sensor(s) (S, 90, 91, 92, 93) being preferably positioned in an
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- effluent portion (54a) of the dialysate fluid circuit, the sensors being in communication with the system processing unit (64) and providing an output indicative of the concentration of the analyte(s) in blood or preferably in spent dialysate fluid; wherein the system processing unit (64) is configured to determine from the output(s) of the sensor(s) (S, 90, 91, 92, 93) a representative blood concentration of the analyte(s), thereby monitoring at least one of GLN_a , $GLUCOSE_a$ and $KETONE_a$.
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10. A therapy set for use in an extracorporeal blood treatment system (50) according to any of claims 1 - 9, the set comprising
- 10 a filtration unit (58) having a membrane (59) which divides an integrated blood line (52a, 52b) and an integrated dialysate fluid line (54a, 54b), wherein the blood line (52a, 52b) and/or the dialysate fluid line (54a, 54b) comprises sensors (S, 90, 91, 92, 93) for monitoring at least one of GLN_a , $GLUCOSE_a$, and $KETONE_a$.
- 15 11. A method of treating a subject suffering from cancer using a system (50) comprising:
- an extracorporeal blood circuit (52a, 52b);
- a dialysate fluid circuit (54a, 54b);
- said extracorporeal blood circuit (52a, 52b) and dialysate fluid circuit (54a, 54b) being divided by a membrane (59) of a filtration unit (58);
- 20 at least one blood pump (60) for controlling the flow of blood through the blood circuit (52a, 52b);
- at least one dialysate fluid pump (62, 68) for controlling the flow of dialysate fluid through the dialysate fluid circuit (54a, 54b);
- and optionally one or more infusion lines (66, 80, 81, 82), each infusion line being connected to the extracorporeal circuit (52a, 52b) or adapted for being directly connected to the vascular system of a subject to be treated, each infusion line comprising an infusion pump;
- 25 wherein the method comprises:
- receiving a concentration value GLN_b representing a desired blood concentration of glutamine (901) within the range of 0.1 and 0.5 mM;
- 30 receiving a concentration value $GLUCOSE_b$ representing a desired blood concentration of glucose (903) within the range of 2 to 4 mM;
- receiving a concentration value $KETONE_b$ representing a desired blood concentration of a ketone body, such as acetoacetate, beta-hydroxybutyrate or pharmaceutically acceptable derivatives esters, and salts thereof (905) within the range of 1 – 15 mM_i;
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- receiving a concentration value GLN_p representing the concentration of glutamine or pharmaceutically acceptable glutamine-containing compounds in the fresh dialysate fluid (902);
- receiving a concentration value $GLUCOSE_p$ representing the concentration of glucose in the fresh dialysate fluid (904);
- optionally, receiving a concentration value $KETONE_{p,i}$ representing the concentration of a ketone body, such as acetoacetate, beta-hydroxybutyrate or pharmaceutically acceptable derivatives, esters and salts thereof in fresh dialysate fluid (907);
- optionally receiving a concentration value $KETONE_i$ representing the concentration of a ketone body such as acetoacetate, beta-hydroxybutyrate or pharmaceutically acceptable derivatives, esters and salts thereof (906), of an infusion liquid to be infused into the extracorporeal blood line (52b) or directly into the vascular system of said subject to be treated, through one of said one or more infusion lines (66, 80, 81, 82);
- receiving a concentration value GLN_a representing the actual concentration of glutamine in the blood of said treated subject (909);
- receiving a concentration value $GLUCOSE_a$ representing the actual concentration of glucose in the blood of said treated subject (910);
- receiving a concentration value $KETONE_a$ representing the actual concentration of a ketone body such as acetoacetate and/or beta-hydroxybutyrate (911);
- controlling said blood pump (60) and said at least one dialysate fluid pump (62, 68) so that the actual concentration value GLN_a of glutamine is driven towards or below GLN_b (912) and the actual concentration value $GLUCOSE_a$ of glucose is driven towards or below $GLUCOSE_b$ (914);
- and
- if the system (50) comprises one or more of said infusion lines (66, 80, 81, 82) and one of said infusion lines (66, 80, 81, 82) infuses said infusion liquid into the extracorporeal blood line (52b) or directly into the vascular system of the subject to be treated, controlling said infusion in such a way that $KETONE_a$ is driven towards $KETONE_b$ (920), or alternatively
- if the system (50) does not infuse any infusion liquid containing a ketone body, the subject to be treated is asked to orally consume an amount of ketone bodies or medium chain triglycerides in case $KETONE_a$ is lower than $KETONE_b$.
12. A method according to claim 11, wherein said system (50) comprises one or more of said infusion lines (66, 80, 81, 82), and wherein the method further comprises

- receiving a concentration value $KETONE_i$ representing the concentration of a ketone body such as acetoacetate, beta-hydroxybutyrate or pharmaceutically acceptable derivatives, esters and salts thereof in an infusion liquid (906);
 infusing said infusion liquid through one of said one or more infusion lines
 5 (66,80,81,82) into the extracorporeal blood line (52b) or directly into the vascular system of the subject to be treated; and
 controlling the infusion pump of said infusion line in such a way that the actual blood concentration value $KETONE_a$ is driven towards $KETONE_b$ (920).
- 10 13. A method according to any one of claim 11 and claim 12, wherein the cancer is selected from human colon carcinoma, and glioblastoma, as well as prostate, breast and liver cancer.
14. A system computing unit (64) adapted for controlling an extracorporeal blood treatment
 15 system (50) for treating a subject suffering from cancer; said system computing unit comprising:
 a plurality of output means adapted for being operatively connected to at least one blood pump (60), at least one dialysate fluid pump (62, 68) and optionally one or more infusion pumps for controlling the flow in each of one or more infusion lines (66, 80, 81,
 20 82);
 a user interface including an input means, and a display means; and
 a memory means and a calculation means;
 the system computing unit (64) being adapted for receiving a desired blood concentration value GLN_b of glutamine (901);
 25 the system computing unit (64) being adapted for receiving a desired blood concentration value $GLUCOSE_b$ of glucose (903);
 the system computing unit (64) being adapted for receiving a desired blood concentration value $KETONE_b$ of a ketone body (905)
 the system computing unit (64) being adapted for receiving a dialysate concentration
 30 value GLN_p of glutamine (902);
 the system computing unit (64) being adapted for receiving a dialysate concentration value $GLUCOSE_p$ of glucose (904);
 optionally, the system computing unit (64) being adapted for receiving a concentration
 35 value $KETONE_p$, representing the concentration of a ketone body, such as acetoacetate, beta-hydroxybutyrate or pharmaceutically acceptable derivatives, esters and salts thereof in fresh dialysate fluid (907);

- optionally, the system computing unit (64) being adapted for receiving an infusion liquid concentration value $KETONE_i$ of a ketone body (906);
- the system computing unit (64) being adapted for receiving an actual blood concentration value GLN_a of glutamine (909);
- 5 the system computing unit (64) being adapted for receiving an actual blood concentration value $GLUCOSE_a$ of glucose (910);
- the system computing unit (64) being adapted for receiving an actual blood concentration value $KETONE_a$ of a ketone body such as beta-hydroxybutyrate and/or acetoacetate (911);
- 10 the system computing unit (64) being adapted for controlling said blood pump (60) and said dialysate fluid pump (62, 68) in such a way that the actual blood concentration value GLN_a of glutamine is driven towards or below GLN_b (912), and the actual blood concentration value $GLUCOSE_a$ of glucose is driven towards or below $Glucose_b$ (914);
- and
- 15 in case an infusion pump is operatively connected to the system computing unit (64), the system computing unit (64) is adapted for controlling the infusion pump in such a way that the actual blood concentration value $KETONE_a$ is driven towards $KETONE_b$ (920);
- and
- 20 in case no infusion pump is operatively connected to the system computing unit (64), the system computing unit (64) is adapted for comparing $KETONE_a$ and $KETONE_b$, and if $KETONE_a < KETONE_b$, displaying a message on said display informing that the treated subject should consume a further amount of ketone bodies or medium chain triglycerides.
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15. A dialysis fluid suitable for dialysis treatment of cancer, comprising ketone bodies such as acetoacetate, beta-hydroxybutyrate or pharmaceutically acceptable derivatives, esters and salts thereof.
- 30 16. A dialysis fluid according to claim 15, further comprising at least one of
- a) glutamine or glutamine-containing compounds; and
- b) glucose.
17. A dialysis fluid according to claim 15, wherein the concentration of:
- 35 a) glutamine or glutamine-containing compounds amounts to 0 – 0.5 mM, and preferably 0.05 – 0.3 mM;
- b) glucose amounts to 0 – 6 mM and preferably 0.5 – 4 mM; and

c) ketone bodies amount to 1 – 15 mM and preferably 2 – 12 mM.