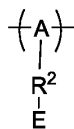


## Claims

1. An enzyme-containing polymer comprising:

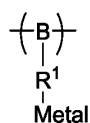
a first repeating unit of Formula Ia:



5

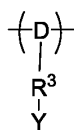
Ia,

a second repeating unit of Formula Ib:



Ib, and

a third repeating unit of Formula Ic:



10

Ic

or conjugate salts thereof, wherein

each of A, B, and D is independently a 2-amino monosaccharide;

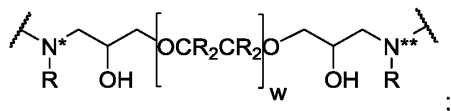
15 E is an enzyme comprising an n-terminal amine and optionally one or more lysine residues, wherein R<sup>2</sup> is covalently bonded to the n-terminal amine or the amine side chain of the one or more lysine residues;

Metal is a metal complex having a redox potential lower than hydrogen peroxide under physiological conditions;

20 R<sup>1</sup> is -N\*(R)(C=O)-, -N\*(R)(C=O)N(R)-, -N\*(R)(CR<sub>2</sub>)<sub>n</sub>-, -N\*(R)(CR<sub>2</sub>)<sub>n</sub>(C=O)-, -N\*(R)(C=O)(CR<sub>2</sub>)<sub>n</sub>-, -N\*(R)(C=O)(CR<sub>2</sub>)<sub>n</sub>(C=O)-, -N\*(R)(CR<sub>2</sub>)<sub>n</sub>O(CR<sub>2</sub>)<sub>m</sub>-, -N\*(R)(CR<sub>2</sub>)<sub>n</sub>S(CR<sub>2</sub>)<sub>m</sub>-, -N\*(R)(CR<sub>2</sub>)<sub>n</sub>O-, -N\*(R)(CR<sub>2</sub>)<sub>n</sub>(C=O)O-, -N\*(R)(C=O)(CR<sub>2</sub>)<sub>n</sub>O-, -N\*(R)(C=O)(CR<sub>2</sub>)<sub>n</sub>(C=O)O-, -N\*(R)(CR<sub>2</sub>)<sub>n</sub>O(CR<sub>2</sub>)<sub>m</sub>O-, -N\*(R)(CR<sub>2</sub>)<sub>n</sub>S(CR<sub>2</sub>)<sub>m</sub>O-, -N\*=CH(CR<sub>2</sub>)<sub>n</sub>-, -N\*=CH(CR<sub>2</sub>)<sub>n</sub>(C=O)-, -N\*=CH(CR<sub>2</sub>)<sub>n</sub>O(CR<sub>2</sub>)<sub>m</sub>-, -N\*=CH(CR<sub>2</sub>)<sub>n</sub>S(CR<sub>2</sub>)<sub>m</sub>-, -N\*=CH(CR<sub>2</sub>)<sub>n</sub>O-, -N\*=CH(CR<sub>2</sub>)<sub>n</sub>(C=O)O-, -N\*=CH(CR<sub>2</sub>)<sub>n</sub>O(CR<sub>2</sub>)<sub>m</sub>O-, or -N\*=CH(CR<sub>2</sub>)<sub>n</sub>S(CR<sub>2</sub>)<sub>m</sub>O-, wherein N\* represents the nitrogen at the  
25 2 position of the 2-amino monosaccharide;

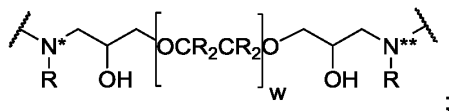
R<sup>2</sup> is -N\*(R)(CR<sub>2</sub>)<sub>n</sub>N\*\*(R)-, -N\*(R)(CR<sub>2</sub>)<sub>n</sub>(C=O)N\*\*(R)-, -N\*(R)(C=O)(CR<sub>2</sub>)<sub>n</sub>-, -N\*(R)(C=O)(CR<sub>2</sub>)<sub>n</sub>(C=O)N\*\*(R)-, -N\*(R)(CR<sub>2</sub>)<sub>n</sub>O(CR<sub>2</sub>)<sub>m</sub>N\*\*(R)-, -N\*(R)(CR<sub>2</sub>)<sub>n</sub>S(CR<sub>2</sub>)<sub>m</sub>N\*\*(R)-,

- 5  $-N^*=CH(CR_2)_nN^{**}(H)-$ ,  $-N^*=CH(CR_2)_n(C=O)N^{**}(R)-$ ,  $-N^*=CH(CR_2)_nO(CR_2)_mN^{**}(R)-$ ,  $-N^*=CH(CR_2)_nS(CR_2)_mN^{**}(R)-$ ,  $-N^*(R)(CR_2)_nCH=N^{**}-$ ,  $-N^*(R)(C=O)(CR_2)_nCH=N^{**}-$ ,  $-N^*(R)(CR_2)_nO(CR_2)_mCH=N^{**}-$ ,  $-N^*(R)(CR_2)_nS(CR_2)_mCH=N^{**}-$ ,  $-N^*=CH(CR_2)_nCH=N^{**}-$ ,  $-N^*=CH(CR_2)_nO(CR_2)_mCH=N^{**}-$ , or  $-N^*=CH(CR_2)_nS(CR_2)_mCH=N^{**}-$ , wherein  $N^*$  represents the nitrogen at the 2 position of the 2-amino monosaccharide and  $N^{**}$  represents the nitrogen of the n-terminal amine or the amine side chain of the one or more lysine residues of the enzyme; or  $R^2$  is



represented by the moiety:

- 10  $R^3$  is  $-N^*(R)(CR_2)_nY$ ,  $-N^*(R)(CR_2)_n(C=O)Y$ ,  $-N^*(R)(C=O)(CR_2)_nY$ ,  $-N^*(R)(C=O)(CR_2)_n(C=O)Y$ ,  $-N^*(R)(CR_2)_nO(CH_2)_mY$ ,  $-N^*(R)(CR_2)_nS(CR_2)_mY$ ,  $-N^*=CH(CR_2)_nY$ ,  $-N^*=CH(CR_2)_n(C=O)Y$ ,  $-N^*=CH(CR_2)_nO(CR_2)_mY$ ,  $-N^*=CH(CR_2)_nS(CR_2)_mY$ ,  $-N^*(R)(CR_2)_nCH=Y$ ,  $-N^*(R)(C=O)(CR_2)_nCH=Y$ ,  $-N^*(R)(CR_2)_nO(CH_2)_mCH=Y$ ,  $-N^*(R)(CR_2)_nS(CR_2)_mCH=Y$ ,  $-N^*=CH(CR_2)_nCH=Y$ ,  $-N^*=CH(CR_2)_nO(CR_2)_mCH=Y$ , or  $-N^*=CH(CR_2)_nS(CR_2)_mCH=Y$ , wherein  $N^*$  represents the nitrogen at the 2 position of the 2-amino monosaccharide; or  $R^3$  is represented by



the moiety:

- 15  $R$  for each occurrence is independently hydrogen, lower alkyl or hydroxyl;  
 $m$  for each occurrence is independently a whole number selected between 1-20;  
 $n$  for each occurrence is independently a whole number selected between 1-20;  
 $w$  for each occurrence is independently a whole number selected between 1-20; and  
 $Y$  is a polyalkylamine comprising at least one metal complex, wherein the polyalkylamine  
 20 optionally crosslinks at least two of the third repeating units.

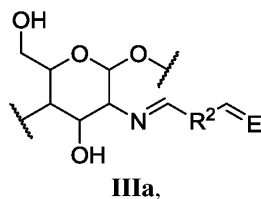
2. The enzyme-containing polymer of claim 1, wherein the metal complex is optionally substituted ferrocenyl.

- 25 3. The enzyme-containing polymer of claim 1, wherein the molar ratio of the first repeating unit to the third repeating unit in the enzyme-containing polymer is between 1:2 to 2:1.

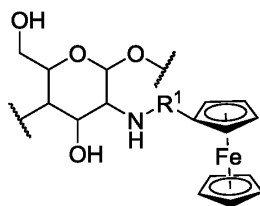
4. The enzyme-containing polymer of claim 1, wherein the 2-amino monosaccharide is selected from the group consisting of glucosamine, mannosamine, and galactosamine.

30

5. The enzyme-containing polymer of claim 2, wherein the first repeating unit has the Formula IIIa:

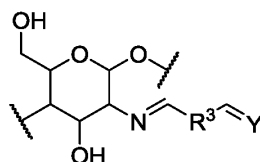


the second repeating unit has the Formula **IIIb**:



**IIIb**, and

the third repeating unit has the Formula **IIIc**:



**IIIc**,

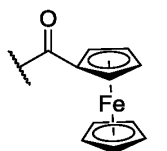
wherein

$R^1$  is  $-(C=O)-$ ,  $-(C=O)(CH_2)_n-$ ,  $-(C=O)(CH_2)_n(C=O)-$ ,  $-(CH_2)_n(C=O)O-$ , or  $-(C=O)(CH_2)_nO-$ ;

10  $R^2$  is  $-(CH_2)_n-$ ;

$R^3$  is  $-(CH_2)_n-$ ; and

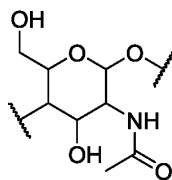
Y is a branched polyethylenimine comprising at least one primary or secondary amine covalently bonded to a moiety having the structure:



15

6. The enzyme-containing polymer of claim 5, wherein  $R^1$  is  $-(C=O)-$ ;  $R^2$  is  $-(CH_2)_3-$ ; and  $R^3$  is  $-(CH_2)_3-$ .

7. The enzyme-containing polymer of claim 5 further comprising a fourth repeating unit of  
20 Formula **IIId**:



**IIId**.

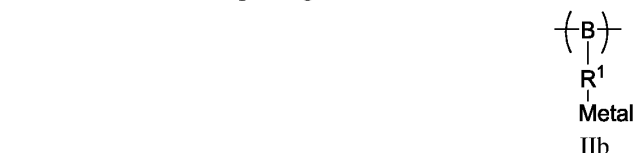
8. The enzyme-containing polymer of claim 5, wherein the enzyme is selected from the group  
25 consisting of glucose oxidase, lactate oxidase, xanthine oxidase, cholesterol oxidase, malate oxidase, galactose oxidase, glucose dehydrogenase, lactate dehydrogenase, xanthine

dehydrogenase, alcohol oxidase, choline oxidase, xanthine oxidase, glutamate oxidase and amine oxidase.

9. A redox polymer comprising a first repeating unit of Formula IIa:



and a second repeating unit of Formula IIb:



or conjugate salts thereof, wherein

each of A and B independently a 2-amino monosaccharide;

Metal is a metal complex having a redox potential lower than hydrogen peroxide under physiological conditions;

15  $\text{R}^1$  is  $-\text{N}^*(\text{R})(\text{C}=\text{O})-$ ,  $-\text{N}^*(\text{R})(\text{C}=\text{O})\text{N}(\text{R})-$ ,  $-\text{N}^*(\text{R})(\text{CR}_2)_n-$ ,  $-\text{N}^*(\text{R})(\text{CR}_2)_n(\text{C}=\text{O})-$ ,  $-\text{N}^*(\text{R})(\text{C}=\text{O})(\text{CR}_2)_n-$ ,  $-\text{N}^*(\text{R})(\text{C}=\text{O})(\text{CR}_2)_n(\text{C}=\text{O})-$ ,  $-\text{N}^*(\text{R})(\text{CR}_2)_n\text{O}(\text{CR}_2)_m-$ ,  $-\text{N}^*(\text{R})(\text{CR}_2)_n\text{S}(\text{CR}_2)_m-$ ,  $-\text{N}^*(\text{R})(\text{CR}_2)_n\text{O}-$ ,  $-\text{N}^*(\text{R})(\text{CR}_2)_n(\text{C}=\text{O})\text{O}-$ ,  $-\text{N}^*(\text{R})(\text{C}=\text{O})(\text{CR}_2)_n\text{O}-$ ,  $-\text{N}^*(\text{R})(\text{C}=\text{O})(\text{CR}_2)_n(\text{C}=\text{O})\text{O}-$ ,  $-\text{N}^*(\text{R})(\text{CR}_2)_n\text{O}(\text{CR}_2)_m\text{O}-$ ,  $-\text{N}^*(\text{R})(\text{CR}_2)_n\text{S}(\text{CR}_2)_m\text{O}-$ ,  $-\text{N}^*=\text{CH}(\text{CR}_2)_n-$ ,  $-\text{N}^*=\text{CH}(\text{CR}_2)_n(\text{C}=\text{O})-$ ,  $-\text{N}^*=\text{CH}(\text{CR}_2)_n\text{O}(\text{CH}_2)_m-$ ,  $-\text{N}^*=\text{CH}(\text{CR}_2)_n\text{S}(\text{CR}_2)_m-$ ,  $-\text{N}^*=\text{CH}(\text{CR}_2)_n\text{O}-$ ,  $-\text{N}^*=\text{CH}(\text{CR}_2)_n(\text{C}=\text{O})\text{O}-$ ,  $-\text{N}^*=\text{CH}(\text{CR}_2)_n\text{O}(\text{CR}_2)_m\text{O}-$ , or  $-\text{N}^*=\text{CH}(\text{CR}_2)_n\text{S}(\text{CR}_2)_m\text{O}-$ , wherein  $\text{N}^*$  represents the nitrogen at the 2 position of the 2-amino monosaccharide;

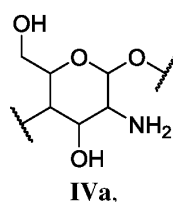
20

R for each occurrence is independently hydrogen or lower alkyl;

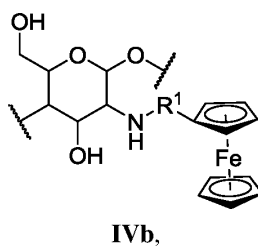
m for each occurrence is independently a whole number selected between 1-20; and

n for each occurrence is independently a whole number selected between 1-20.

25 10. The redox polymer of claim 9, wherein the first repeating unit has the Formula IVa:



and the second repeating unit has the Formula IVb:



wherein

$R^1$  is  $-(C=O)-$ ,  $-(C=O)(CH_2)_n-$ ,  $-(C=O)(CH_2)_n(C=O)-$ ,  $-(CH_2)_n(C=O)O-$ , or  $-(C=O)(CH_2)_nO-$ .

- 5 11. The redox polymer of claim 10, wherein  $R^1$  is  $-(C=O)-$ .
12. A sensor, comprising:  
a substrate;  
a first sensor electrode on the substrate;  
a first sensing layer on the first sensor electrode, the first sensing layer comprising a first  
10 enzyme-containing polymer as defined in any one of claims 1 to 8; and  
a reference electrode on the substrate.
13. The sensor according to claim 12, further comprising:  
a second sensor electrode on the substrate; and  
15 a second sensing layer on the second sensor electrode, the second sensing layer comprising  
a second enzyme-containing polymer as defined in any one of claims 1 to 8.
14. The sensor according to claim 12 or 13, wherein the first sensing layer or the second  
sensing layer has a thickness of in the range of about 0.010 mm to about 0.300 mm.
- 20 15. The sensor according to any one of claims 12 to 14, further comprising:  
an elongated body portion having a body axis extending centrally through the elongated  
body portion; and  
a tip portion having a tip axis extending centrally through the tip portion, the tip portion  
comprising the substrate,  
25 wherein the tip portion is disposed adjacent the elongated body portion and at an obtuse  
angle of between  $90^\circ$  to  $170^\circ$  between the body axis and the tip axis.
16. The sensor according to claim 15, wherein the elongated body portion comprises a fluid  
reservoir and an actuator, and the tip portion further comprises an inflatable member, wherein a  
30 channel is disposed between the fluid reservoir and the inflatable member, and wherein the actuator  
is configured to deliver a volume of fluid in the fluid reservoir through the channel to the inflatable  
member to inflate the inflatable member.
17. The sensor according to claim 15, wherein the elongated body portion comprises a securing  
35 pin and the tip portion further comprises a moveable member, and wherein the securing pin is  
configured to secure the moveable member at an activated position
18. A monitor, comprising:  
a receiver module configured to receive a sensor output of a sensor as defined in any one of  
40 claims 12 to 17 and a control output of another sensor as defined in any one of claims 12 to 17;  
a processor module configured to receive a first metabolite concentration value  
corresponding to the sensor output and a first control value corresponding to the control output  
from the receiver module, wherein the processor module is configured to:  
compare the first metabolite concentration value against the first control value; and  
45 generate a first alarm signal on a condition that a difference between the first metabolite  
concentration value and the first control value is above a first pre-determined value.

19. The monitor according to claim 18, wherein the processor module is further configured to receive a second metabolite concentration value corresponding to the sensor output and a second control value corresponding to the control output from the receiver module, and wherein the processor module is further configured to:
- 5       compare the second metabolite concentration value against the second control value; and  
      generate a second alarm signal on a condition that a difference between the second metabolite concentration value and the second control value is above a second pre-determined value.
- 10   20. The monitor according to claim 19, wherein the processor module is further configured to trigger an alarm on a condition that the first alarm signal and/or the second alarm signal is generated, the alarm indicating a possibility of tissue failure.
21. The monitor according to claim 19 or 20, further comprising an output module in communication with the processor module, wherein the output module is configured to provide an indication of at least one of:
- 15       the first metabolite concentration value;  
      the first control value;  
      the second metabolite concentration value;  
      the second control value;  
20       the difference between the first metabolite concentration value and the first control value;  
      the difference between the second metabolite concentration value and the second control value;  
      the difference between the first metabolite concentration value and the first control value with respect to the first pre-determined value; and  
25       the difference between the second metabolite concentration value and the second control value with respect to the second pre-determined value.
22. A method of manufacturing a sensor, comprising:
- 30       providing a substrate;  
      forming a first sensor electrode on the substrate;  
      forming a first sensing layer on the first sensor electrode, the first sensing layer comprising a first enzyme-containing polymer as defined in any one of claims 1 to 8; and  
      forming a reference electrode on the substrate.
23. The method according to claim 22, further comprising:
- 35       forming a second sensor electrode on the substrate; and  
      forming a second sensing layer on the second sensor electrode, the second sensing layer comprising a second enzyme-containing polymer as defined in any one of claims 1 to 8.
24. A method for monitoring failure of a tissue on a patient, comprising the steps of:
- 40       (i) providing a first sensor according to claims 12 to 17 on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;  
      (ii) providing a second sensor according to claims 12 to 17 on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;

- (iii) providing a third sensor according to claims 12 to 17 on or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;
- 5 (iv) providing a fourth sensor according to claims 12 to 17 on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;
- (v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time; and
- 10 (vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time,
- wherein an at least 10% decrease in the amount of said first metabolite as measured by said first sensor as compared to the amount of said first metabolite as measured by said second sensor; and

15 at least 10% increase in the amount of said second metabolite as measured by said third sensor as compared to the amount of said second metabolite as measured by said fourth sensor,

is indicative that said tissue is prone to failure.

25. A monitor, comprising:
- a receiver module configured to receive a sensor output of a sensor according to claims 12 to 17 and a control output of another sensor according to claims 12 to 17;
- 20 a processor module configured to receive a first metabolite concentration value corresponding to the sensor output and a first control value corresponding to the control output from the receiver module, wherein the processor module is configured to:
- compare the first metabolite concentration value against the first control value; and generate a first alarm signal on a condition that a difference between the first metabolite concentration value and the first control value is above a first pre-determined value.
- 25

26. The monitor according to claim 25, wherein the processor module is further configured to receive a second metabolite concentration value corresponding to the sensor output and a second control value corresponding to the control output from the receiver module, and wherein the processor module is further configured to:
- 30 compare the second metabolite concentration value against the second control value; and generate a second alarm signal on a condition that a difference between the second metabolite concentration value and the second control value is above a second pre-determined value.

27. The monitor according to claim 25, wherein the difference between the first metabolite concentration value and the first control value is at least 10% different from the first pre-determined value.
- 35

28. The monitor according to claim 26, wherein the difference between the second metabolite concentration value and the second control value is at least 10% different from the second pre-determined value.

29. A method for monitoring failure of a tissue on a patient, comprising the steps of:
- 40 (i) providing a first sensor according to claims 12 to 17 on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;

- 5 (ii) providing a second sensor according to claims 12 to 17 on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;
- (iii) providing a third sensor according to claims 12 to 17 on or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;
- 10 (iv) providing a fourth sensor according to claims 12 to 17 on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;
- (v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time; and
- (vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time,
- 15 wherein an at least 10% decrease in the amount of said first metabolite as measured by said first sensor as compared to the amount of said first metabolite as measured by said second sensor; and
- at least 10% increase in the amount of said second metabolite as measured by said third sensor as compared to the amount of said second metabolite as measured by said fourth sensor,
- is indicative that said tissue is prone to failure.

- 20 30. A method for monitoring failure of a tissue on a patient, comprising the steps of:
- (i) providing a first sensor according to claims 12 to 17 on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;
- (ii) providing a second sensor according to claims 12 to 17 on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;
- 25 (iii) providing a third sensor on according to claims 12 to 17 or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;
- (iv) providing a fourth sensor according to claims 12 to 17 on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;
- 30 (v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time; and
- 35 (vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time,
- wherein the amount of said first metabolite as measured by said first sensor and the amount of said first metabolite as measured by said second sensor are substantially the same; and
- at least 10% increase in the amount of said second metabolite as measured by said third sensor as compared to the amount of said second metabolite as measured by said fourth sensor,
- 40 is indicative that said tissue is prone to failure.

31. A method for monitoring failure of a tissue on a patient, comprising the steps of:

- 5 (i) providing a first sensor according to claims 12 to 17 on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;
- (ii) providing a second sensor according to claims 12 to 17 on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;
- 10 (iii) providing a third sensor according to claims 12 to 17 on or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;
- (iv) providing a fourth sensor according to claims 12 to 17 on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;
- 15 (v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time; and
- (vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time,
- wherein an at least 10% decrease in the amount of said first metabolite as measured by said first sensor as compared to the amount of said first metabolite as measured by said second sensor; and
- 20 the amount of said second metabolite as measured by said third sensor and the amount of said second metabolite as measured by said fourth sensor are substantially the same,
- is indicative that said tissue is prone to failure.

32. A method for monitoring failure of a tissue on a patient, comprising the steps of:

- 25 (i) providing a first sensor according to claims 12 to 17 on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;
- (ii) providing a second sensor according to claims 12 to 17 on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;
- 30 (iii) providing a third sensor on according to claims 12 to 17 or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;
- (iv) providing a fourth sensor according to claims 12 to 17 on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;
- 35 (v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time; and
- (vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time,
- 40 wherein an at least 10% decrease in the amount of said first metabolite as measured by said first sensor as compared to the amount of said first metabolite as measured by said second sensor; and
- an at least 10% decrease in the amount of said second metabolite as measured by said third sensor as compared to the amount of said second metabolite as measured by said fourth sensor,
- is indicative that said tissue is prone to failure.

33. A method for monitoring failure of a tissue on a patient, comprising the steps of:

- (i) providing a first sensor according to claims 12 to 17 on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;
- 5 (ii) providing a second sensor according to claims 12 to 17 on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;
- (iii) providing a third sensor according to claims 12 to 17 on or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;
- 10 (iv) providing a fourth sensor according to claims 12 to 17 on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;
- (v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time; and
- 15 (vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time,

wherein an at least 10% increase in the amount of said first metabolite as measured by said first sensor as compared to the amount of said first metabolite as measured by said second sensor; and

- 20 an at least 10% increase in the amount of said second metabolite as measured by said third sensor as compared to the amount of said second metabolite as measured by said fourth sensor,

is indicative that said tissue is prone to failure.