

Claims:

We claim:

The invention claimed is:

1. A method of ablating undesirable soft tissue, comprising the steps of:

identifying a location of said soft tissue within said subject;

determining a position of at least one electrode relative to said soft tissue;

introducing said at least one electrode to said position within said subject, said electrode electrically connected to a controller for controlling the delivery of electric pulses to said electrode, said controller comprising an electric pulse generator;

applying to said soft tissue an electric field, said electric field applied to said soft tissue by delivering from said pulse generator to said at least one electrode at least one bi-polar electric pulse configured to cause said electrical membrane breakdown;

said at least one bi-polar electric pulse being characterized by a bipolar wave form having an instant charge reversal between a positive and negative polarity of each cycle;

wherein said frequency of said electric field is from 100 kHz to 450 kHz.

2. The method of claim 1 wherein a voltage of said at least one bi-polar electric pulse is from 0.5kV to 10 kV and a frequency of said electric field is from 14.2 kHz to less than 500 kHz.

3. The method of claim 2 wherein said voltage over time of said bi-polar electric pulse traces a square waveform for a positive and negative component of a polarity oscillation.

4. The method of claim 1 wherein the duration of said at least one bi-polar electric pulse is from 100-1000 μ s.

5. The method of claim 1, wherein said determining step further comprises the steps of estimating or measuring the dielectric constant and the conductivity of said soft tissue.
6. The method of claim 1 wherein said electric field applied to said soft tissue by said pulse generator comprises at least one bipolar pulse train comprising a series of not less than 100 bipolar pulses, each said bipolar pulse in said series separated by an inter pulse burst interval during which no voltage is applied to said at least one electrode.
7. The method of claim 6, further comprising the step of configuring said series of electric pulses delivered to said at least one electrode from said pulse generator to apply said electric field, wherein said electric field causes no clinically significant thermal damage to said soft tissue.
8. The method of claim 7, wherein said series of electric pulses is configured to apply a field that causes a temperature of said soft tissue to rise to not more than 50 degrees Celsius.
9. The method of claim 6, further comprising the step of delivering from said pulse generator to said at least one electrode a second bipolar pulse train comprising a second series of electric pulses delivered so as to apply to said soft tissue a second electric field.
10. The method of claim 9, further comprising the step of configuring said second series of electric pulses to apply said second electric field to cause clinically significant thermal damage to said soft tissue.

11. The method of claim 6, further comprising the steps of delivering from said pulse generator to said at least one electrode a second bipolar pulse train comprising a second series of electric pulses configured to cause a temperature of at least a portion of said tissue to exceed 50 degrees Celsius.

12. The method of claim 6,

wherein a tissue change, cellular membrane destruction and cell death are visually observable in a sample of said undesirable soft tissue taken immediately after applying said electric field to said soft tissue; and further comprising the steps of,

after applying said electric field to said soft tissue by delivering said series of electric pulses, immediately biopsying a portion of said soft tissue to determine an efficacy of said ablation;

if said efficacy exceeds a pre-determined threshold, ceasing said ablation of undesirable soft tissue; and

if said efficacy does not exceed said pre-determined threshold, delivering from said pulse generator to said at least one electrode a second at least one bi-polar electric pulse so as to apply to said soft tissue a second electric field.

13. The method of claim 12 wherein said second at least one bi-polar electric pulse is a second bipolar pulse train comprising a series of not less than 100 electric pulses configured so that said second electric field is sufficient to cause electrical membrane breakdown of said cell membrane of a plurality of cells of said soft tissue.

14. The method of claim 12 wherein said second at least one bi-polar electric pulse is configured so that said second electric field causes a temperature of at least a portion of said tissue to exceed 50 degrees Celsius.

15. The method of claim 12 wherein said second electric field causes a temperature of at least a portion of said tissue to exceed 60 degrees Celsius but not to exceed 95 degrees Celsius.

16. The method of claim 1, further comprising the step of introducing a temperature probe proximal to said at least one electrode, said probe operatively connected to said controller and reporting a temperature reading to said controller, said controller controlling varying at least one character of said at least one bi-polar electric pulse in response to said reported temperature.

17. The method of claim 16, wherein said temperature probe is a thermocouple.

18. The method of claim 16, wherein said temperature probe is integral to said at least one electrode and introduced therewith.

19. The method of claim 16, wherein said at least one bi-polar electric pulse is a bipolar pulse train comprising a series of not less than 100 bipolar pulses separated by an inter pulse burst interval during which no voltage is applied to said at least one electrode; and further comprising the steps of

storing in a memory of said controller at least one temperature set-point; and

altering by said controller for at least a portion of said series at least one of a pulse duration, said inter pulse burst interval and a total number of pulses in said series in response to said temperature reading reported to said controller from said probe exceeding said set point.

20. The method of claim 19, further comprising the step of initiating said altering step in response to said temperature reported by said probe falling below said set-point.

21. The method of claim 19, wherein said altering step comprises reducing said pulse duration.

22. The method of claim 20, wherein said altering step comprises increasing said inter pulse burst interval.

23. The method of claim 21, wherein said altering step comprises reducing the number of pulses in said series.

24. The method of claim 1, further comprising the steps of

storing in a memory of a controller at least one maximum current set-point, said controller controlling said delivery of at least one bi-polar electric pulse;

determining by said controller a current through said at least one electrode; and

reducing said voltage of said at least one bi-polar electric pulse delivered to said at least one electrode when said current equals said maximum current set-point whereby said current is prevented from exceeding said set point.

25. The method of claim 1 wherein said intracellular components and internal constituent part of said cell membrane are left in said extracellular space of said subject wherein an immunologic process of said subject is activated to remove said intracellular components and internal constituent part of said cell membrane from said extracellular space.

26. The method of claim 25 wherein said intracellular components comprises a cellular antigen and said internal constituent part of said cell membrane further comprises a cell membrane specific antigen; and

wherein said immunologic process further comprises removal of undesirable soft tissue at a second location in said living subject having one or more of said cellular antigen and said cell membrane specific antigen, said undesirable soft tissue at a second location in said living subject not having undergone said method of ablating undesirable soft tissue.

27. The method of claim 25 wherein said intracellular components comprises a cellular antigen and said internal constituent part of said cell membrane further comprises an antigen specific to said cell membrane; and

further comprising the step of, after said step of applying to said soft tissue an electric field, administering to said subject an immunologic response enhancing drug to increase said immunologic process of said subject is activated to remove said intracellular components and internal constituent part of said cell membrane from said extracellular space.

28. The method of claim 27 wherein said immunologic response enhancing drug blocks inhibition of the CTLA-4 inhibitory signal of cytotoxic lymphocytes.

29. The method of claim 27 wherein said immunologic response enhancing drug is administered by one of intravenously, orally and intramuscularly.

30. The method of claim 27 wherein said immunologic response enhancing drug is injected directly into or adjacent to undesirable soft tissue before or after said step of applying to said soft tissue an electric field.

31. The method of claim 27 wherein said immunologic response enhancing drug is comprised of autologous dendritic cells.

32. The method of claim 27 wherein said immunologic response enhancing drug binds to S100A9 and modulating regulatory myeloid cell functions.

33. The method of claim 27 wherein said immunologic response enhancing drug is comprised of autologous dendritic cells.

34. The method of claim 1, further comprising the steps of:

inserting one or more sensors into said soft tissue within said subject;

obtaining a plurality of measurements from said sensors simultaneously with said step of applying to said soft tissue an electric field sufficient to cause electrical membrane breakdown of a cell membrane of a plurality of cells; and

determining, based on said measurements, a treatment efficacy of said method of ablating undesirable soft tissue in a living subject.

35. The method of claim 34, wherein at least one of said one or more sensors is chosen from the group comprising a pH sensor, a lactate sensor, a glucose sensor, an electrical impedance sensor, a potassium sensor, a uric acid sensor, and a spectrometer.

36. The method of claim 34, further comprising altering one or more parameters of said electric field based on said treatment efficacy.

37. A method of ablating undesirable soft tissue, comprising the steps of:

identifying a location of said soft tissue within said subject;

determining based on a tissue type of said soft tissue a minimum energy profile necessary to be applied to a cell of said soft tissue to cause cell membrane rupture by electrical membrane breakdown;

determining a position of at least one electrode relative to said cell mass;

introducing said at least one electrode to said position within said subject, said electrode electrically connected to a controller for controlling the delivery of electric pulses to said electrode, said controller comprising an electric pulse generator;

determining based on said minimum energy profile and said position of said at least one electrode an electric field strength necessary to apply to said cell mass said minimum energy profile;

determining based on said electric field strength a bi-polar electric pulse train profile having not less than 100 pulses, said pulse train profile characterized by a pulse number, pulse duration and inter pulse burst intervals, said pulses each having a frequency and a voltage, said voltage characterized by an instantaneous reversal of polarity;

delivering from said pulse generator to said at least one electrode by said controller a series of electric pulses according to said electric pulse train profile whereby a pulsed electric

field is generated, said field applying sufficient energy to a plurality of said cells of said soft tissue to cause cell death by electrical membrane breakdown;

wherein said frequency of said electric field is from 100 kHz to 450 kHz.

38. The method of claim 27 wherein said immunologic response enhancing drug blocks a protein selected from the group comprising PD-1 and PD-L1.

39. A method of increasing an immunologic response, comprising the steps of:

identifying a location of undesirable soft tissue within said subject;

performing a non-thermal ablation treatment on said undesirable soft tissue, said non-thermal ablation treatment comprising applying to said soft tissue an electric field; and

administering an immunologic response enhancing drug to said subject.

40. The method of claim 39, wherein said step of performing a non-thermal ablation treatment further comprises

determining a position of at least one electrode relative to said undesirable soft tissue;

introducing said at least one electrode to said position within said subject, said electrode electrically connected to a controller for controlling the delivery of electric pulses to said electrode, said controller comprising an electric pulse generator; and

applying to said soft tissue an electric field sufficient to cause electrical membrane breakdown of a cell membrane of a plurality of cells of said soft tissue to cause immediate spillage of all intracellular components into an extracellular space and exposure of an internal constituent part of said cell membrane to said extracellular space, said electric field applied to said soft tissue by delivering from said pulse generator to said at least one electrode at least one bi-polar electric pulse configured to cause said electrical membrane breakdown.

41. The method of claim 39, wherein said immunologic response enhancing drug blocks a protein selected from the group comprising PD-1 and PD-L1.

42. The method of claim 39, wherein said immunologic response enhancing drug blocks inhibition of the CTLA-4 inhibitory signal of cytotoxic lymphocytes.