Extrusion Methods and Devices for Drug Delivery

TECHNICAL FIELD

[0001] *In general, the disclosed embodiments relate to methods and devices for the introduction and subsequent evaluation of agents to solid tissue, and in particular to the simultaneous introduction of a plurality of agents to the tissue in vivo.*

BACKGROUND

[0002] The cost of new drug development from discovery through phase III trials is estimated to be between $800 million and $1.7 billion and the process can take between eight and ten years. Despite success in classical anticancer models, many cancer therapeutics do not reach the clinic. Numerous drug candidates fail during clinical trials. It is estimated that more than 90% of cancer-related therapeutics will fail phase I or II clinical trial evaluation. The failure rate in phase III trials is almost 50%.

[0003] There is a need in the art for improved methods and devices for delivering and evaluating cancer therapeutics. The present invention addresses these and needs, and offer other related advantages.

SUMMARY OF THE INVENTION

In one aspect, there is provided a device for delivering one or more agents to a solid tissue, comprising:

a. two or more needles, wherein said two or more needles comprise a first end and a second end;

b. a reservoir, wherein said reservoir is in fluid communication with said first end of said two or more needles;

c. a plunger, wherein said plunger is coupled to said reservoir; and

d. a controller, wherein said controller controls a rate of fluid delivery, wherein withdrawal of at least one of said two or more needles from said solid tissue occurs simultaneously with delivery of at least one of said one or more agents to said solid tissue.

In one aspect, the disclosure provides a device for delivering one or more agents to a solid tissue, comprising:

(a) two or more needles, wherein said two or more needles comprise a first end and a second end;

(b) a reservoir, wherein said reservoir is in fluid communication with said first end of said two or more needles;

(c) a plunger, wherein said plunger is coupled to said reservoir; and

(d) a controller, wherein said controller controls a rate of fluid delivery,

wherein said device is configured to withdraw at least one of said two or more needles from said solid tissue and simultaneously deliver at least one of said one or more agents to said solid tissue, and wherein said device is configured to deliver a substantially equal amount of said one or more agents at any given location along a length of said at least one of said two or more needles.

In one aspect, the disclosure provides for a device, comprising a top block having a first plurality of holes sized to allow a needle to pass through the top block and a bottom block having a second plurality of holes sized to allow a needle to pass through the bottom block, wherein the top and bottom blocks are in a substantially parallel arrangement and wherein the first and second plurality of holes are positioned so as to allow one or more needles to pass through a hole in the top block and the bottom block in a path substantially vertical to the plane of both blocks. In some embodiments, the device further comprises at least one adjustable leg, wherein the at least one adjustable leg is attached to the bottom block. In some embodiments, there are four adjustable legs. In some embodiments, the at least one leg is vertically and horizontally adjustable. In some embodiments, the bottom block is stationary. In some embodiments, the top block moves vertically relative to the bottom block. In some embodiments, the top block moves along guide rods attached to the bottom block. In some embodiments, the device further comprises a system to control vertical movement of the top block. In some embodiments, the first and second plurality of

CLAIMS

WHAT IS CLAIMED IS:

1. A device for delivering one or more agents to a solid tissue, comprising:

a. two or more needles, wherein said two or more needles comprise a first end and a second end;

b. a reservoir, wherein said reservoir is in fluid communication with said first end of said two or more needles;

c. a plunger, wherein said plunger is coupled to said reservoir; and

d. a controller, wherein said controller controls a rate of fluid delivery, wherein withdrawal of at least one of said two or more needles from said solid tissue occurs simultaneously with delivery of at least one of said one or more agents to said solid tissue.

2. The device of claim 1, wherein said two or more needles are positioned in an array.

3. The device of claim 2, wherein said array comprises 5 or more needles.

4. The device of claim 3, wherein each of said 5 or more needles comprises a different agent.

5. The device of claim 2, wherein at least two of said two or more needles comprises a same agent at different concentrations.

6. The device of claim 1, wherein at least one of said one or more agents comprises an anti-cancer agent.

7. The device of claim 6, wherein said anti-cancer agent comprises a small molecular agent.

8. The device of claim 1, wherein at least one of said one or more agents comprises a position marker.

9. The device of claim 1, wherein at least one of said one or more agents comprises a negative control.

10. The device of claim 1, wherein at least one of said one or more agents comprises a positive control.

11. The device of claim 1, wherein at least one of said one or more agents is delivered to said solid tissue at a therapeutically effective concentration.

12. The device of claim 1, wherein at least one of said one or more agents is delivered to said solid tissue in an amount that is undetectable outside said solid tissue.

13. The device of claim 1, wherein at least one of said one or more agents is delivered to said solid tissue at a therapeutically effective concentration, and wherein outside said solid tissue said at least one of said one or more agents is present at a concentration that is undetectable.

14. The device of claim 1, wherein said solid tissue comprises a tumor.

15. The device of claim 1, wherein at least one of said one or more agents comprises a chemotherapeutic.

16. The device of claim 1, wherein at least one of said one or more agents comprises tattoo ink.

17. The device of claim 1, wherein at least one of said two or more needles delivers said one or more agents by passive delivery.

18. The device of claim 1, wherein a rate of said withdrawal of said at least one of said two or more needles is controlled by said controller.

19. The device of claim 1, wherein a portion of said one or more agents is delivered when a needle is not being withdrawn from said solid tissue.

20. The device of claim 1, wherein said one or more agents are delivered to said solid tissue only during said withdrawal of said at least one of said two or more needles from said solid tissue.

21. The device of claim 1, wherein said one or more agents are delivered in a column.

22. The device of claim 21, wherein a length of said column is between about 1 to about 10 millimeters.

23. The device of claim 1, wherein said rate of delivery of said one or more agents is at least 0.1 microliter/minute.

24. The device of claim 1, wherein said rate of delivery of said one or more agents is in the range of about 0.4 to about 4 microliters/minute.

25. The device of claim 18, wherein said rate of needle withdrawal is at least 0.1 mm/min.

26. The device of claim 18, wherein said rate of needle withdrawal is in the range of about 0.5 to about 5 mm/min.

Claims

1. A device for delivering one or more agents to a solid tissue, comprising:

(a) two or more needles, wherein said two or more needles comprise a first end and a second end;

(b) a reservoir, wherein said reservoir is in fluid communication with said first end of said two or more needles;

(c) a plunger, wherein said plunger is coupled to said reservoir; and

(d) a controller, wherein said controller controls a rate of fluid delivery,

wherein said device is configured to withdraw at least one of said two or more needles from said solid tissue and simultaneously deliver at least one of said one or more agents to said solid tissue, and wherein said device is configured to deliver a substantially equal amount of said one or more agents at any given location along a length of said at least one of said two or more needles.

2. The device of claim 1, wherein said two or more needles are positioned in an array.

3. The device of claim 2, wherein said array comprises 5 or more needles.

4. The device of claim 3, wherein each of said 5 or more needles comprises a different agent.

5. The device of claim 2, wherein at least two of said two or more needles comprises a same
agent at different concentrations.

6. The device of claim 1, wherein at least one of said one or more agents comprises an anti-cancer agent.

7. The device of claim 6, wherein said anti-cancer agent comprises a small molecular agent.

8. The device of claim 1, wherein at least one of said one or more agents comprises a position marker.

9. The device of claim 1, wherein at least one of said one or more agents comprises a negative control.

10. The device of claim 1, wherein at least one of said one or more agents comprises a positive control.

11. The device of claim 1, wherein at least one of said one or more agents is delivered to said solid tissue at a therapeutically effective concentration.

12. The device of claim 1, wherein at least one of said one or more agents is delivered to said

solid tissue in an amount that is undetectable outside said solid tissue.

13. The device of claim 1, wherein at least one of said one or more agents is delivered to said solid tissue at a therapeutically effective concentration, and wherein outside said solid tissue said at least one of said one or more agents is present at a concentration that is undetectable.

14. The device of claim 1, wherein said solid tissue comprises a tumor.

15. The device of claim 1, wherein at least one of said one or more agents comprises a chemotherapeutic.

16. The device of claim 1, wherein at least one of said one or more agents comprises tattoo ink.

17. The device of claim 1, wherein at least one of said two or more needles delivers said one or more agents by passive delivery.

18. The device of claim 1, wherein a rate of said withdrawal of said at least one of said two or more needles is controlled by said controller.

19. The device of claim 1, wherein a portion of said one or more agents is delivered when a needle is not being withdrawn from said solid tissue.

20. The device of claim 1, wherein said one or more agents are delivered to said solid tissue only during said withdrawal of said at least one of said two or more needles from said solid tissue.

21. The device of claim 1, wherein said one or more agents are delivered in a column.

22. The device of claim 21, wherein a length of said column is between about 1 to about 10 millimeters.

23. The device of claim 1, wherein said rate of delivery of said one or more agents is at least 0.1 microliter/minute.

24. The device of claim 1, wherein said rate of delivery of said one or more agents is in the range of about 0.4 to about 4 microliters/minute.

25. The device of claim 18, wherein said rate of needle withdrawal is at least 0.1 mm/min.

26. The device of claim 18, wherein said rate of needle withdrawal is in the range of about 0.5 to about 5 mm/min.