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Development of Simulation Models of Respiratory Tracking and Synchronizing for Radiotherapy

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Remarkable advances have been made in radiotherapy for cancer. Tumors inside the body that move with respiration can now be tracked during irradiation or can be irradiated at a specific phase of respiration [1]. Since radiation of these wavelengths is invisible to the human eye, it is not possible to see whether a tumor that is moving during respiration is being irradiated accurately. Therefore, simulations that use the actual respiration wave to show the tumor being irradiated are useful for training and to explain the procedure to patients.

Introduction

Radiation generated by radiotherapy equipment has a dosage rate, which is defined as the strength over time. Therefore, the duration of irradiation of a tumor inside the body at a certain dose is determined by the dose rate. For tumors in the brain, head, and neck region, fixing the target area in place can prevent tumor movement during irradiation. However, with tumors of the lung or abdomen, the displacement of the organs during respiration is substantial, and the tumor moves with respiration during the irradiation time. In conventional radiotherapy, respiratory displacement of the tumor is taken into account by targeting a large radiation field. However, when a large radiation field is used, the large radiation dose delivered to the patient in one session can cause severe side effects; thus, irradiation has to be carried out over a longer period with smaller doses.

For small tumors located inside the brain, precise irradiation of a small field has been shown to enable delivery of a single large dose without adverse side effects. An attempt has been made to apply this technology to tumors of the trunk, where the most important issue is countering the respiratory movement of the tumor. One way to achieve this is to detect respiratory displacement and conduct irradiation according to the positional information. One such method is to carry out irradiation when the tumor is in position within a certain range, and another method is to track respiratory displacement during irradiation. Revolutionary advances in radiation therapy technology have enabled both these methods to be used in practice [1].

Depicting the form of irradiation of a small tumor inside the body with countermeasures against respiratory movement in a three-dimensional simulation could promote better understanding of this therapeutic method. In the simulation, a target volume is set to encompass the shape of a small tumor. The tumor moves along the vertical axis of the trunk (Y axis). For irradiation, either the radiation field moves in accordance with the tumor movement, or irradiation is performed only when the tumor has completely entered the radiation field in a set respiratory phase. At the same time, the respiration wave is output and the position of the tumor on that waveform is recreated.

Collecting Position Information of the Respiration Wave

Respiratory displacement was sampled at a rate of 25 times/s using a pressure sensor attached to the body. The sampled data was stored in a CSV file to be read into *Mathematica*. The read-in data is shown in the output of the list plot below. In the graph, the minimum value on exhalation during free respiration was defined as 0, and the maximum value on inhalation was defined as 100.

Acquired Respiration Data

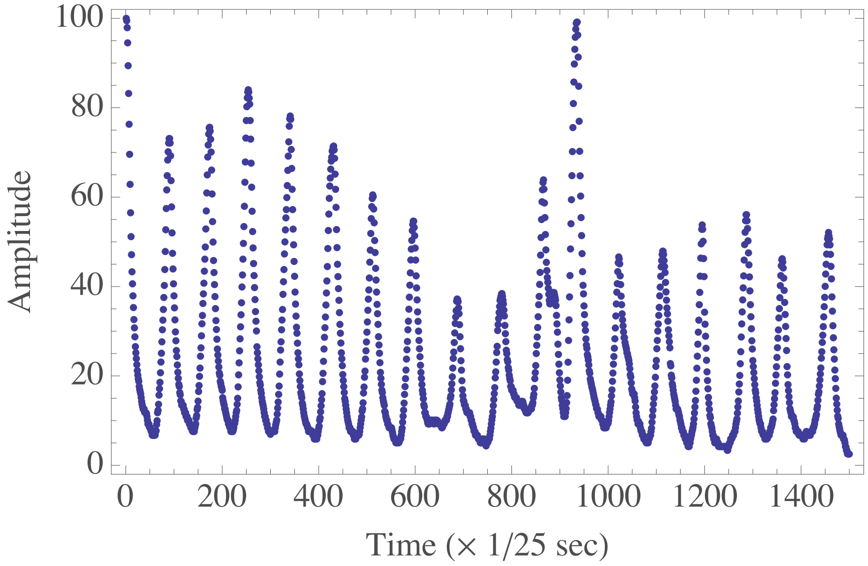
The notebook defines 3407 triplets.

Respiration Wave

This extracts the respiration wave data and plots it.

```
wave = Take[First /@ Rest[RespData], 1500];
```

```
ListPlot[wave, Frame → True,
 FrameStyle → Directive[GrayLevel[0.3], 14],
 FrameLabel → {"Time (× 1/25 sec)", "Amplitude"}]
```



■ Simulation of a Small Tumor inside the Body

A single malignant tumor cell generated by the effects of carcinogenic factors at several stages forms a visible tumor mass through continued monoclonal proliferation. Cell density is high in the center of the tumor and is assumed to spread out in three dimensions in a normal distribution.

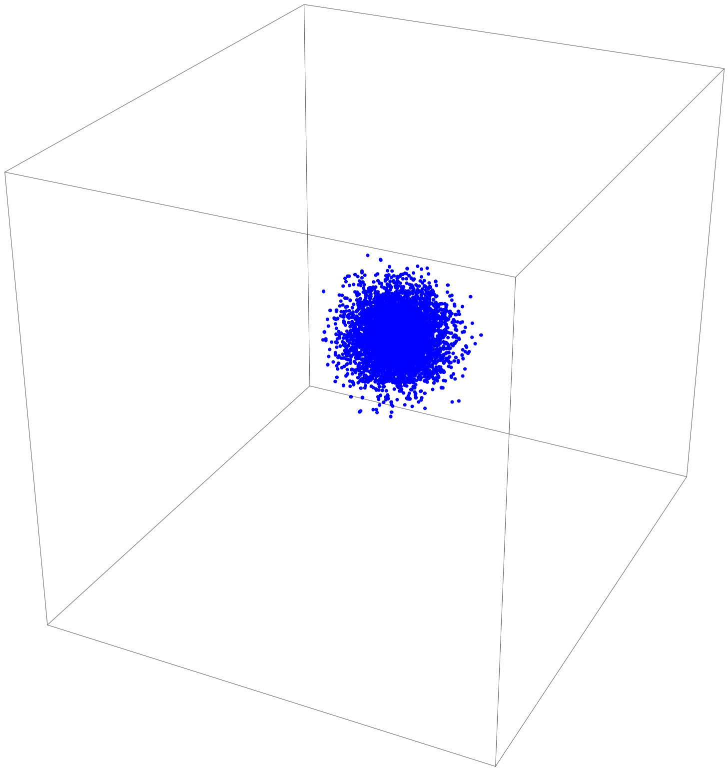
This defines the 3D normal distribution of tumor morphology.

```
tP[m_, s_, k_] := RandomReal[NormalDistribution[m, s], k]
```

This defines the location of the tumor at a given time with a given color.

```
tumor[color_, t_] :=
 Graphics3D[{PointSize[0.005], color,
   Point[
    Transpose[{tP[0, 10, 5000], tP[-wave[[t]], 10, 5000],
      tP[0, 10, 5000]}]]},
  PlotRange → {{-100, 100}, {-160, 70}, {-100, 100}},
  ImageSize → 300]
```

```
tumor[Blue, wave[[1]]]
```



A Tumor that Moves with Time

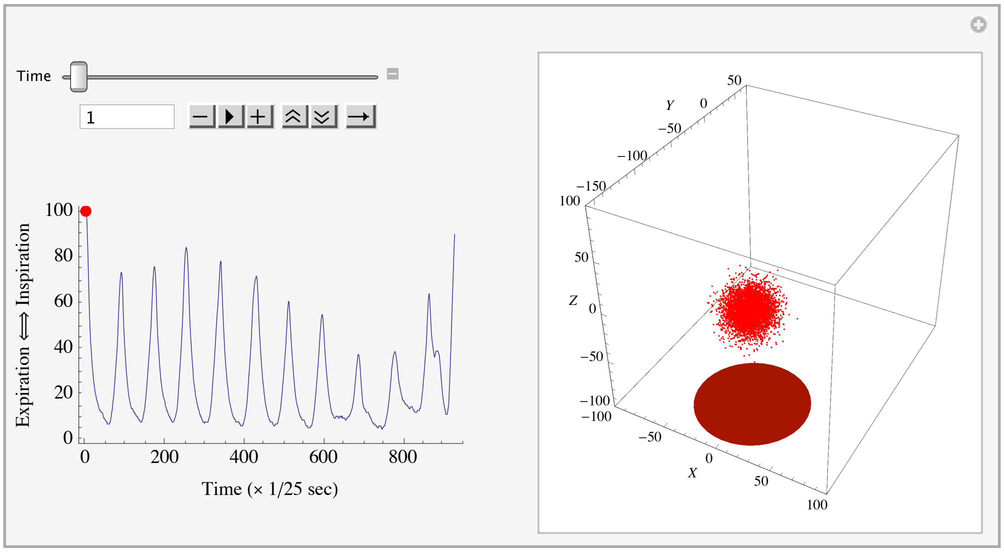
The center of the tumor moves along the Y axis with amplitude given by the respiratory wave and shown on the left with a red point. Think of the front of the body as the front plane (the plane parallel to the X-Z given by $Y = -150$).

Irradiating by Tracking Respiration

The patient is lying on the surface of the bed (with respect to the graph, the patient lies on the X-Y plane with the head in the negative Y direction, the feet in the positive Y direction, and looking up in the Z direction). As the patient breathes, the tumor moves in the direction of the length of the body (i.e. along the Y axis). A tumor-tracking beam acts on the X-Y plane set at five times the standard deviation of the tumor spread. The beam moves with the respiratory wave in the same way as the tumor.

```
(* Beam alignment *)
beam[t_] :=
 Graphics3D[{Blend[{Red, Yellow}, .1], CapForm["Butt"],
   Tube[{{0, -abC[[t]], -100}, {0, -wave[[t]], -99.9}}, 50]},
  PlotRange → {{-100, 100}, {-160, 70}, {-100, 100}}]

Manipulate[Show[{tumor[Red, t], beam[t]},
  Axes → {True, True, True}, AxesLabel → {X, Y, Z},
  ImageSize → 250],
 {{t, 1, "Time"}, 1, 930, 1, AnimationRate → 25,
  Appearance → "Open"},
 Dynamic[
  Show[{ListLinePlot[Take[wave, 930]],
    Graphics[{PointSize[Large], Red,
      Point[{t, wave[[t]]}]}]},
   PlotRange → {{0, 930}, {0, 100}}, Ticks → {True, True},
   Frame -> {{True, False}, {True, False}},
   FrameStyle → Directive[Black, 12],
   FrameLabel → {"Time (× 1/25 sec)",
     "Expiration ⟺ Inspiration"}, ImagePadding → 40,
   ImageSize → 320]], SaveDefinitions → True,
 ControlPlacement → Left]
```



□ Respiratory-Synchronized Irradiation

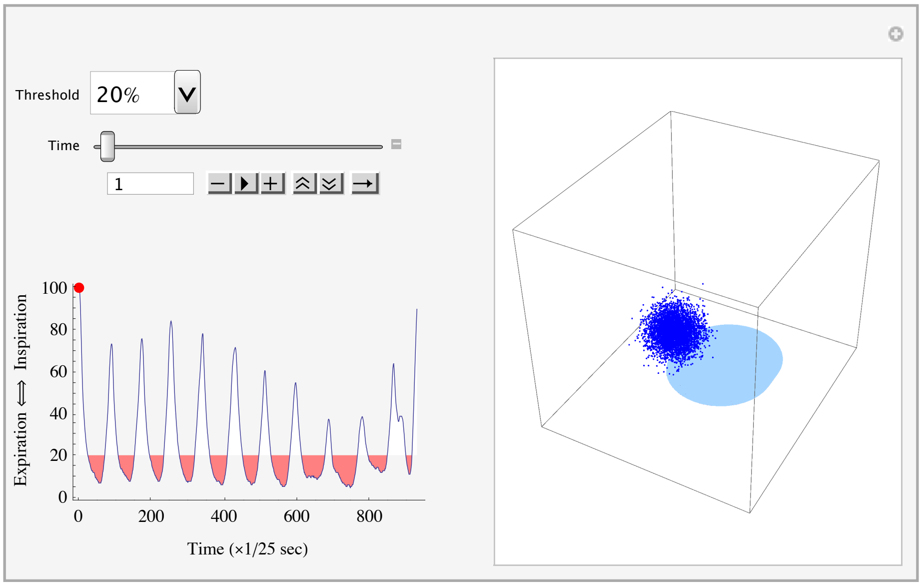
In this situation, the beam is set to turn on when it enters a set position in the respiratory wave amplitude (“Threshold *k*”). On and off gating of the radiation beam is easily observable on the respiratory waveform, the *k*% threshold value being clearly indicated.

```
(* Tumor Movement *)
abcTumor[col_, t_] :=
 Graphics3D[{PointSize[0.005], col,
   Point[Transpose[{tP[0, 10, 5000], tP[-abC[[t]], 10, 5000],
      tP[0, 10, 5000]}]]},
  PlotRange → {{-100, 100}, {-160, 70}, {-100, 100}},
  ImageSize → 200]

(* Beam alignment *)
abcBeam[col_, k_] :=
 Graphics3D[
  Table[{col, CapForm["Butt"],
    Tube[{{0, -i, -100}, {0, -i, -99.99}}, 50]}, {i, 0, k}],
  PlotRange → {{-100, 100}, {-160, 70}, {-100, 100}}, ,
  ImageSize → 200]
```

This shows the irradiation synchronized to respiration.

```
Manipulate[If[
  Take[abC, 930][[t]] ≤ k,
  Show[{abcTumor[Red, t],
    abcBeam[Blend[{Red, Yellow}, 1 / 5], k]}, ImageSize → 250],
  Show[{abcTumor[Blue, t], abcBeam[White, k]},
   ImageSize → 250]
 ], {{k, 20, "Threshold"},
  {0 → "RT(-)", 10 → "10%", 20 → "20%", 30 → "30%",
   40 → "40%", 50 → "50%", 60 → "60%", 70 → "70%",
   80 → "80%", 90 → "90%", 100 → "100%"}},
 {{t, 1, "Time"}, 1, 930, 1, AnimationRate → 25,
  Appearance → "Open"},
 Dynamic[
  Show[{ListPlot[Take[abC, 930], Joined → True,
      Filling → {1 -> {k, {Pink, White}}}],
     Graphics[{PointSize[Large], Red,
       Point[{t, abC[[t]]}]}]},
   PlotRange → {{0, 930}, {0, 100}}, Ticks → {True, True},
   Frame -> {{True, False}, {True, False}},
   FrameStyle → Directive[Black, 12],
   FrameLabel → {"Time (×1/25 sec)",
     "Expiration ⟺ Inspiration"}, ImagePadding → 40,
   ImageSize → 320]], Delimiter, ControlPlacement → Left,
 SaveDefinitions → True]
```



Threshold 20%

Time 1

■ Discussion

Stereotactic radiotherapy was originally developed for the treatment of diseased regions inside the cranium, which do not move once fixed in position. It has been demonstrated that targeting a small lesion from multiple directions enables delivery of a large radiation dose in one session, without causing side effects to the adjacent normal tissue. To apply this technology to tumors in the trunk region, which move in conjunction with respiration, the tumor needs to be immobilized. An attempt was made to irradiate the tumors from multiple directions with minimized respiratory movement by fixing the body in position and compressing the abdomen to reduce the movement of the diaphragm to very slight movement [2, 3]. This method was shown to be safe and effective and represents a technological innovation in stereotactic irradiation of the trunk region. Having patients hold their breath during irradiation is the simplest method, which is becoming widespread—a method equivalent to stereotactic radiotherapy used for the cranium. On the other hand, irradiation conducted under free-breathing conditions is the most appropriate physiological method, but requires a mechanism for irradiating during a phase synchronized with the respiratory wave [4, 5]. Moreover, the method of irradiating the tumor while tracking its movement with respiration has presented difficulties in controlling the motion of a movable section of the irradiation equipment [6, 7]. However, recent advances in irradiation equipment and control computers have now enabled both of these methods to be utilized.

To make these complicated therapies understandable is difficult with only written descriptions and static images. We have therefore attempted to develop a dynamic simulation model based on actual respiratory wave data. This simulation model has been well received by students and medical residents and is also effective in explaining the procedure to patients.

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