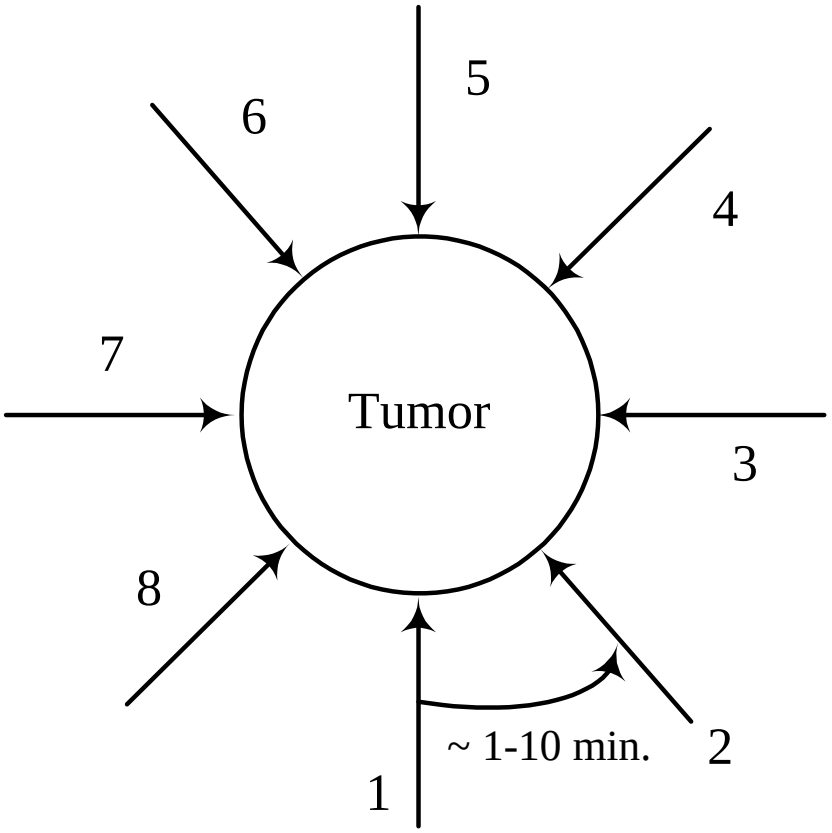
Treatment Fraction Optimization

- 3-dimensional external beam treatment methods (e.g., IMRT) may use as many as 10 to 20 patient-beam orientations to deliver a treatment fraction.
- May take from 15 minutes to 2 hours to deliver a dose fraction.
- Cells experience small “pulses” of radiation separated in time by a few seconds up to as much as 10 to 20 minutes.



Radiation Therapy Treatment

HeLa S3 Cervix Carcinoma Cells

```
<!
  HELA S3 CERVIX CARCINOMA TUMOR CELLS
  PJ Deschavanne et al, Radiat. Res., 122(1),
  29-37   (1990).
  DATE: 20-APR-2000
!>

CELL DNA=4682.0D+06
IRAD CL=3.0108733E+00   FL=3.1519581E-01
CLRP RHT=2.0           BMR=3.3293680E-03
SOLVER DBLV=0 ETOL=1.0E-09 MXSS=999999 HMAX=24.0
SIMCON FSDX=0 TSAX=10 TCUT=150 RCUT=1.0D-09

<!
30 day treatment delivered using a single patient-beam
orientations.  Dose fractions are delivered on weekdays only.  The
size of each dose fraction is adjusted so that the treatments from
35 to 70 Gy are delivered using the same temporal pattern (the
duration of each radiation pulse is adjusted to modify the size of
the treatment fraction).
!>
  XBRT  NTD=30 TTD=RX1 TD4F=2 OPT=3 WDO=Y
  XBTF  ADR=1000
  RX1 = 35 40 45 50 55 60 65 70  /
```

Radiation Therapy Treatment

HeLa S3 Cervix Carcinoma Cells

```
<!
  HELA S3 CERVIX CARCINOMA TUMOR CELLS
  PJ Deschavanne et al, Radiat. Res., 122(1),
  29-37   (1990).
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!>

CELL DNA=4682.0D+06
IRAD CL=3.0108733E+00   FL=3.1519581E-01
CLRP RHT=2.0           BMR=3.3293680E-03
SOLVER DBLV=0 ETOL=1.0E-09 MXSS=999999 HMAX=24.0
SIMCON FSDX=0 TSAX=10 TCUT=150 RCUT=1.0D-09

<!
30 day treatment delivered using a 10 patient-beam orientations.
It takes 6 minutes to move between patient-beam orientations and
dose fractions are delivered on weekdays only.  The size of each
dose fraction is adjusted so that the treatments from 35 to 70 Gy
are delivered using the same temporal pattern (the duration of each
radiation pulse is adjusted to modify the size of the treatment
fraction).
!>
XBRT  NTD=30 TD4F=2 TTD=RX1 OPT=3 WDO=Y
XBTF  ADR=1000 NBD=10 RBI=RX2 TTO=6
RX1 = 35 40 45 50 55 60 65 70  /
RX2 = 1 1 1 1 1 1 1 1 1 1 /
```
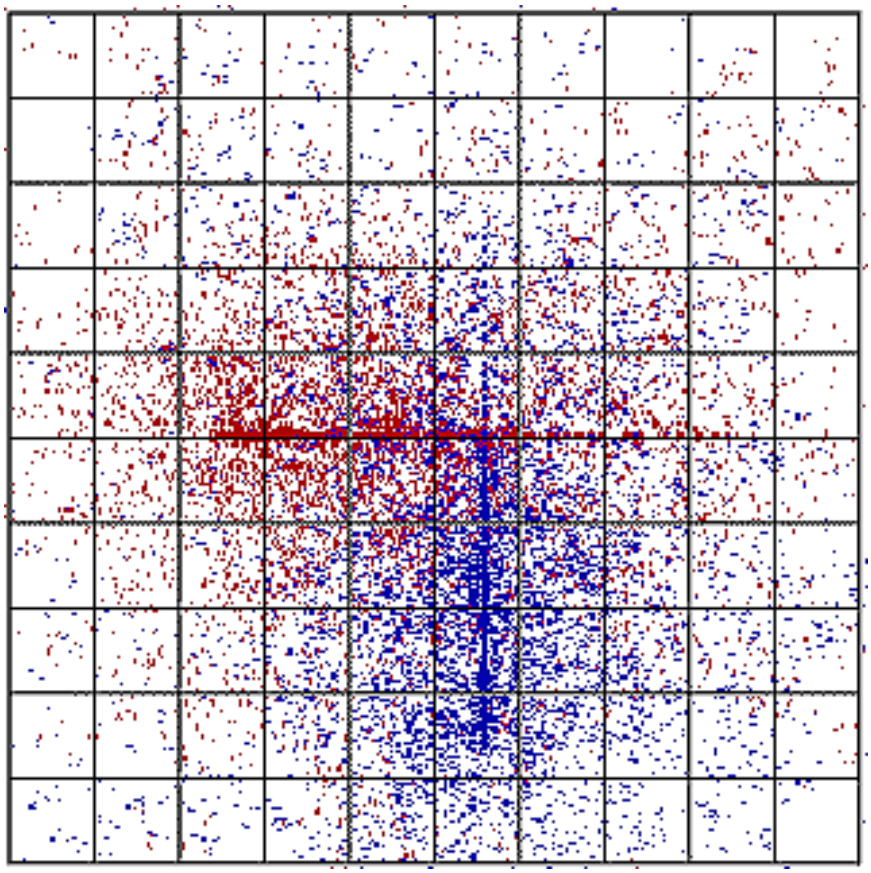
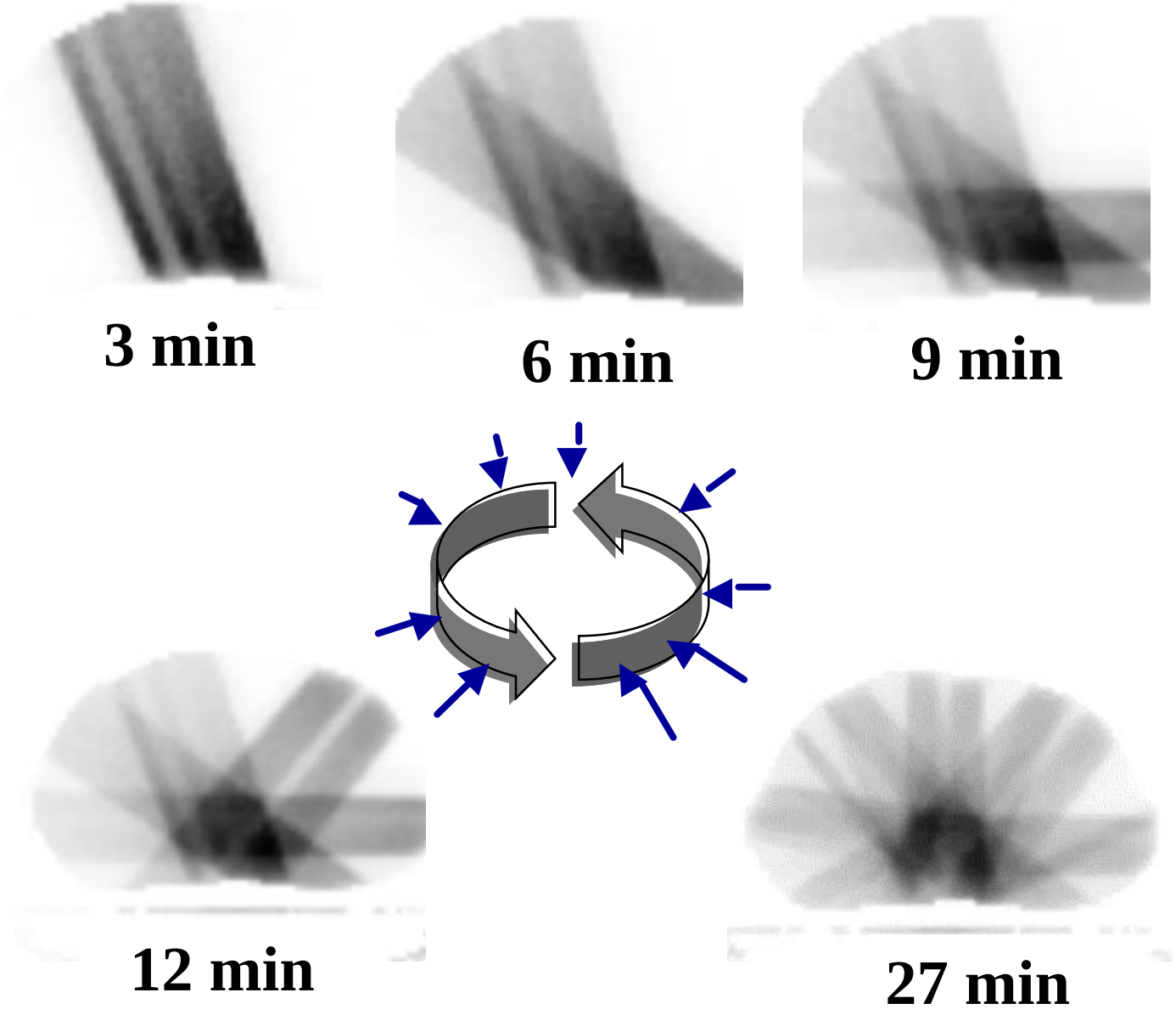

What about beam attenuation in the tumor?

Orthographic projection into a plane of the energy deposits created in water by two monodirectional, 1 MeV photon pencil beams oriented perpendicular to each other. The area of the rectangular regions is 100 cm^2.



Monte Carlo transport calculations were performed using an EGS4 application developed by RD Stewart.

9 Beam Intensity-Modulated Radiation Treatment



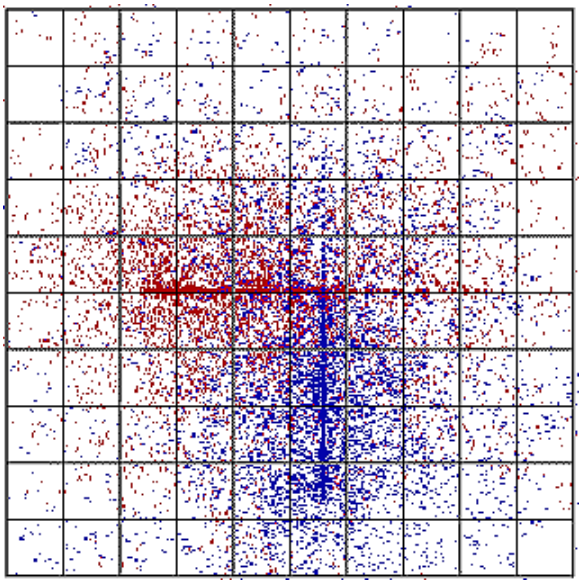
EGS4 Monte Carlo transport in a patient-specific voxel construct courtesy of Dr. CM Ma (Stanford University School of Medicine).

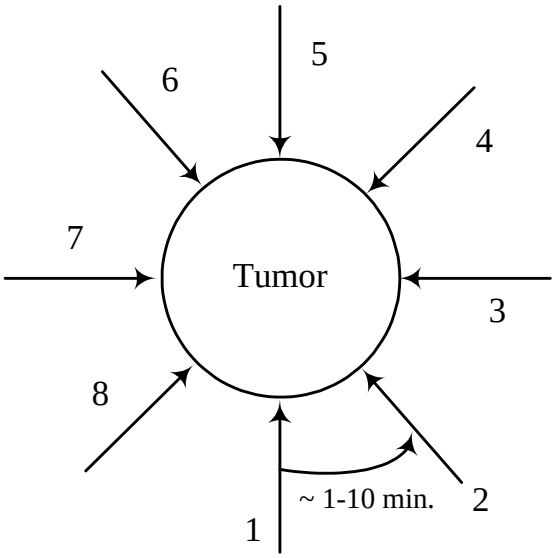
Conclusions

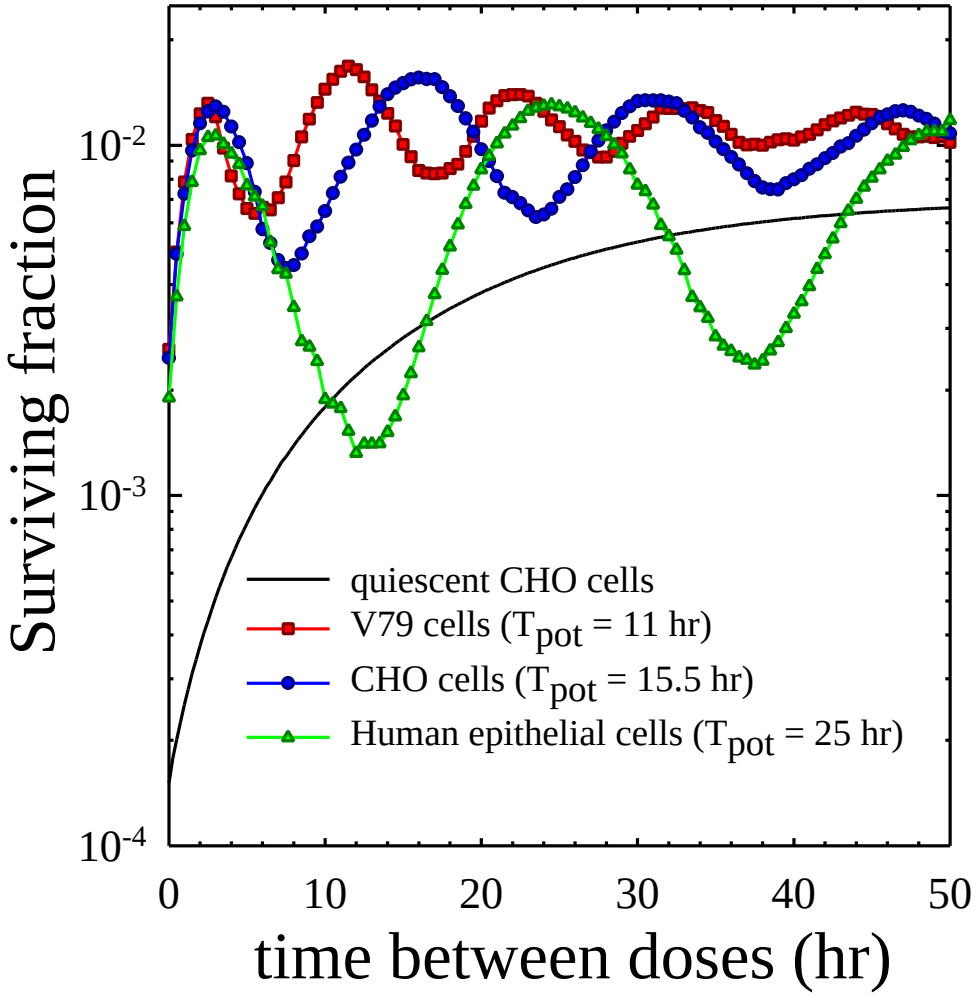
- Dose protraction effects tend to reduce cell killing as
  - number of beam directions increases.
  - delivery time increases.
- Importance of dose protraction effects increases rapidly as the size of the dose fractions increases.
- Magnitude of the dose protraction effect may be on the order of
  - 15 to 70% for delivery times less than 0.5 h.
  - a factor of **3 to 10** for a 1-2 h dose fraction delivery time and
- Beam attenuation in the tumor and intensity modulation may further reduce cell killing by factors on the order of
  - 5 to 25% for delivery times less than 0.5 h.
  - 25 to 55% for delivery times less than 1-2 h.

Opportunities?

- Patient-beam sequence optimization might improve treatment effectiveness.
  - Select a sequence of patient-beam orientations that minimizes the total dose-fraction delivery time (***no brainer***).
  - Selectively target different regions of the tumor (different set of beams) on different treatment days or at different times on the same day (***high-risk, high-payoff***).
  - Select a sequence of patient-beam orientations that maximizes tumor cell killing and minimizes normal tissue damage regardless of the overall delivery time (***high-risk, high-payoff***).





Temporal Optimization of a Series of Dose Fractions – *A Few Remarks*

- Dose fraction delivery timed to take advantage of tumor and/or normal tissue proliferation kinetics.
  - All treatment fractions delivered at prescribed times.
  - Two large treatment doses delivered at prescribed times followed by a more standard treatment regimen.
  - Preferentially target certain sections of the tumor with paired, dose fractions at prescribed times.