Chromosome Aberrations Induced by Charged Particles

- Biodosimetry
- Certain cancers are associated with specific types of chromosome aberrations
- Large target size
- Information on DNA repair/misrepair and repair kinetics

Ground base accelerator facilities

- Loma Linda University

  Protons, 250 MeV

- BNL

  Fe, 1 GeV/u, 600 MeV/u

  Others

- NIRS, Chiba, Japan

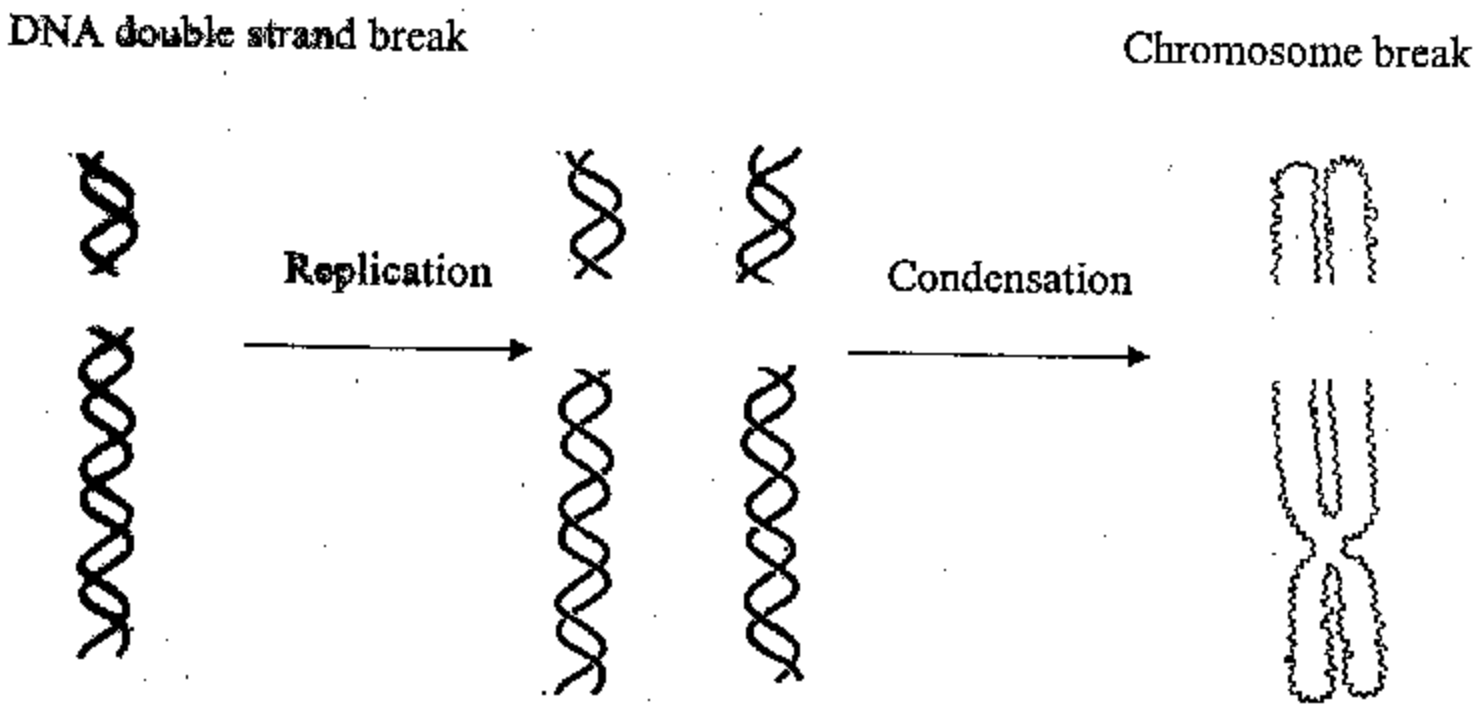
  C, 290 MeV/u

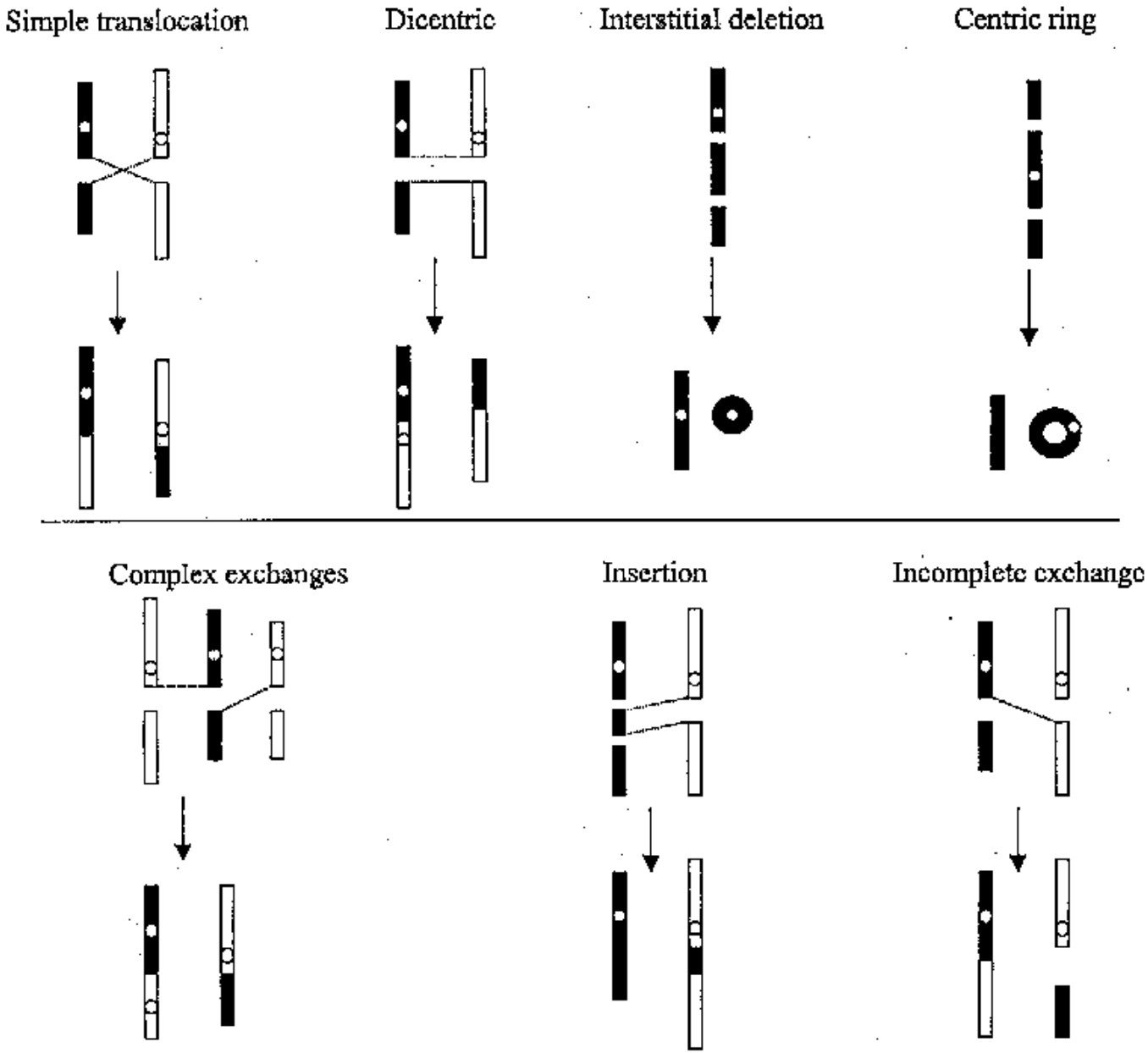
  Si, 400 MeV/u

  Ar, 550 MeV/u

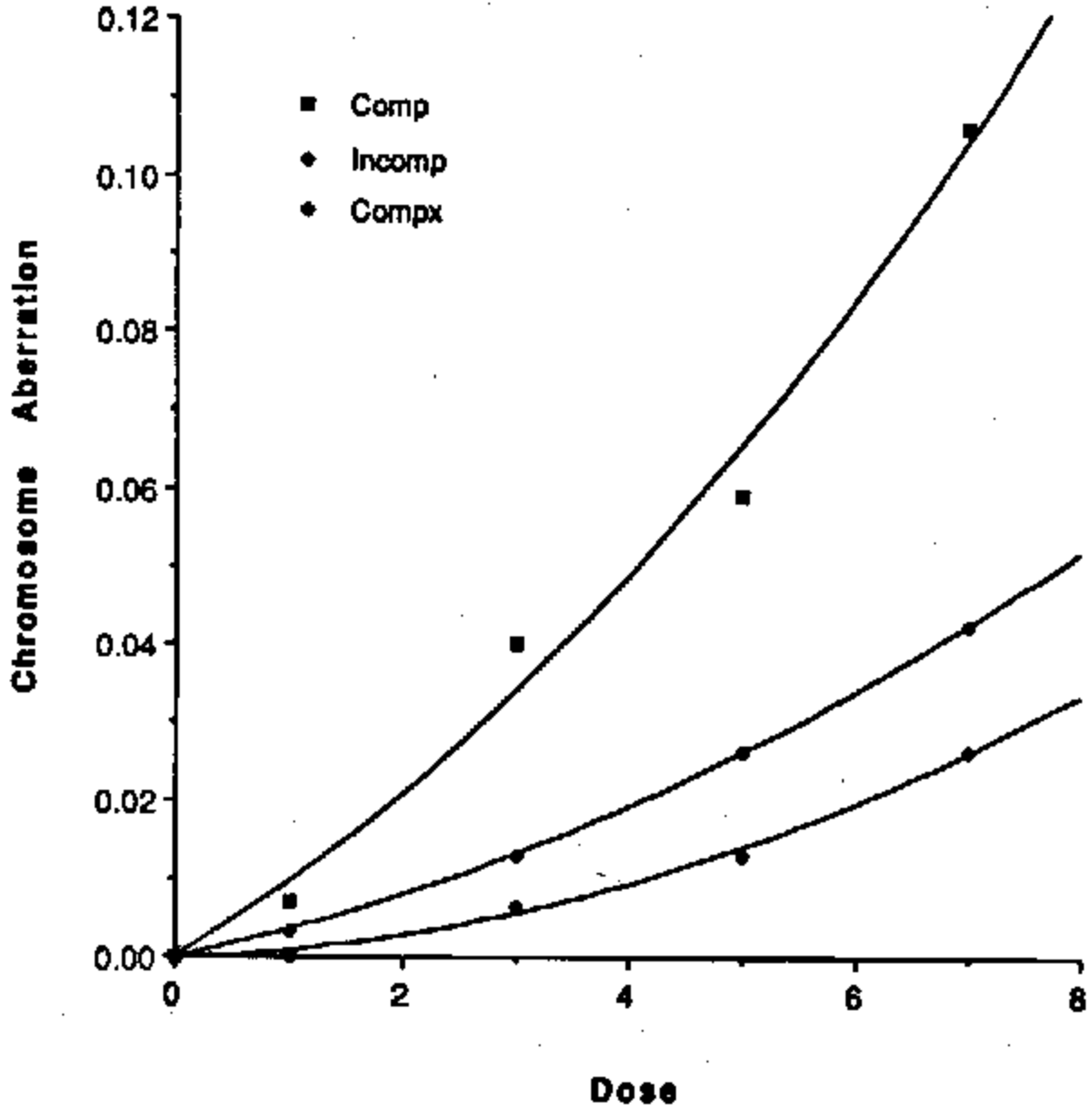
  Fe, 200 MeV/u

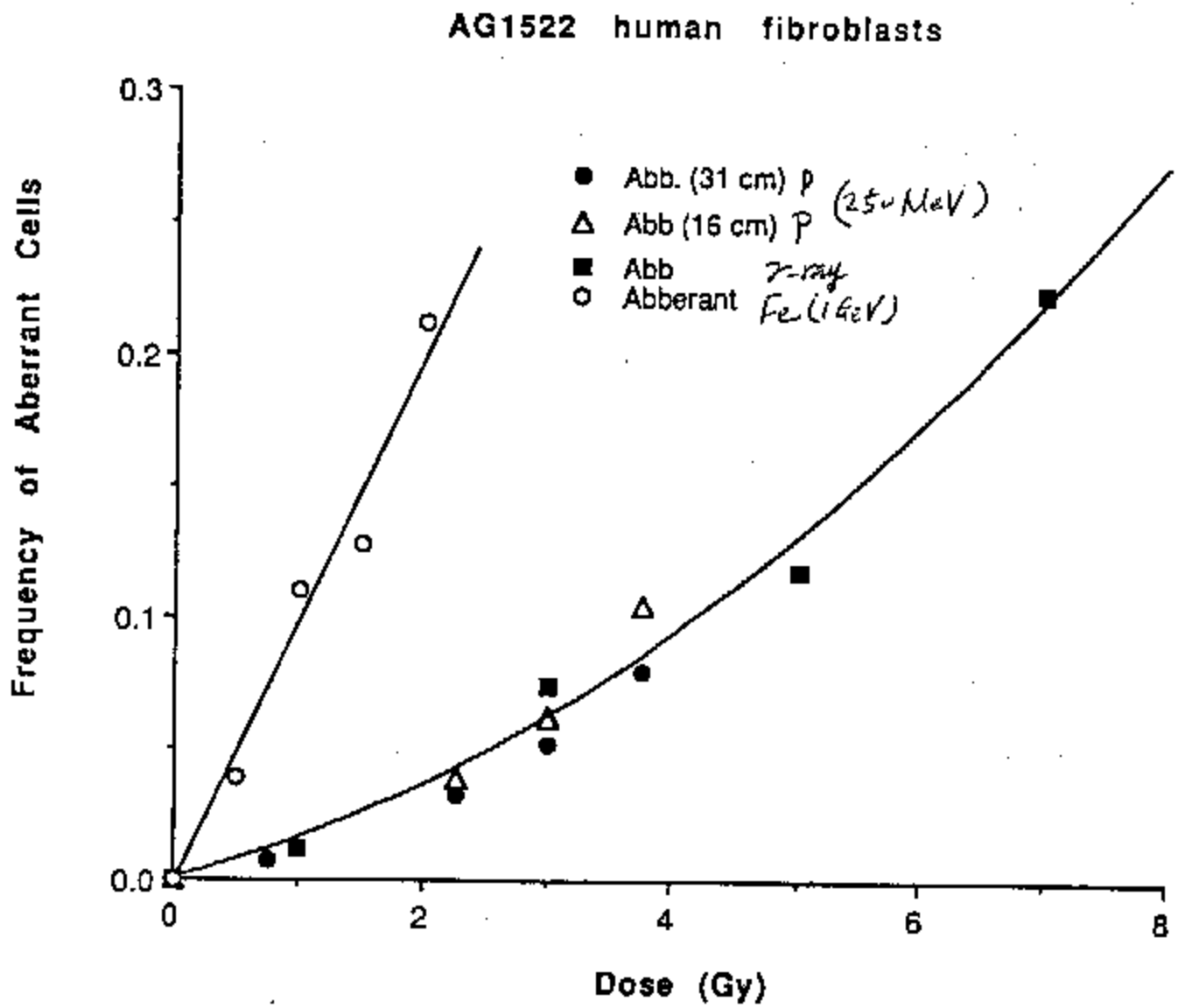
  Others

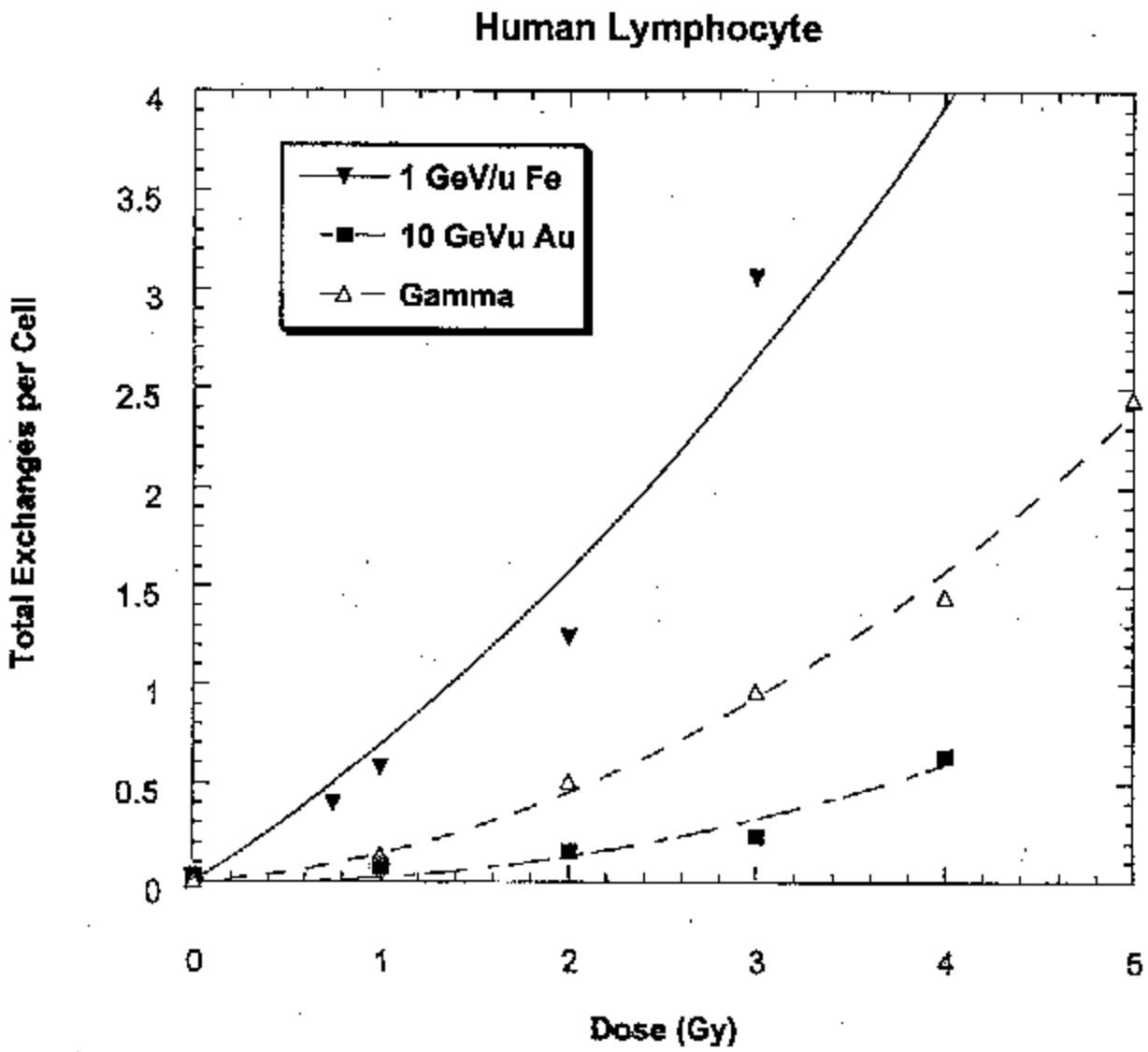

DNA double strand break
Replication
Condensation
Chromosome break

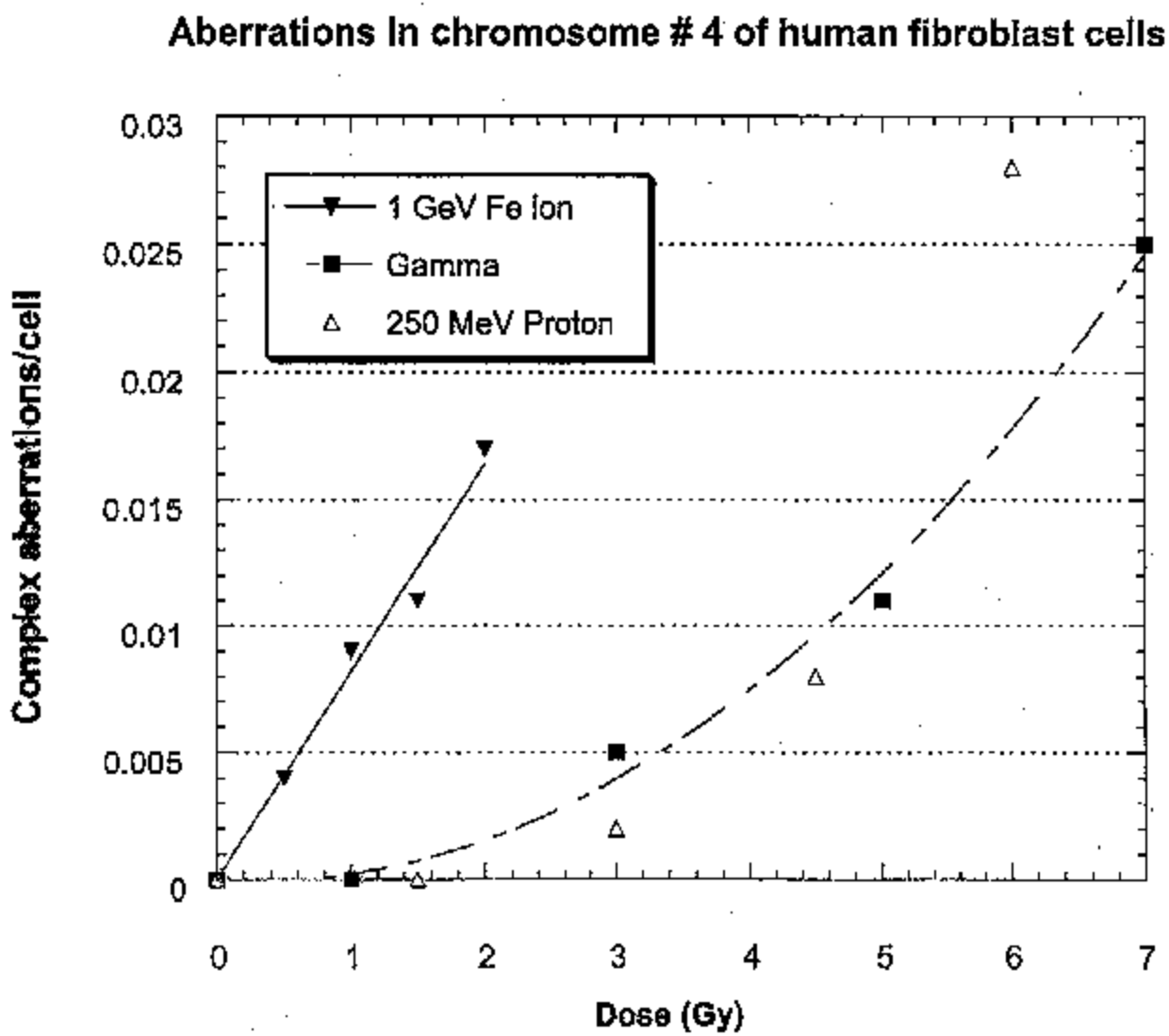

Simple translocation
Dicentric
Interstitial deletion
Centric ring
Complex exchanges
Insertion
Incomplete exchange

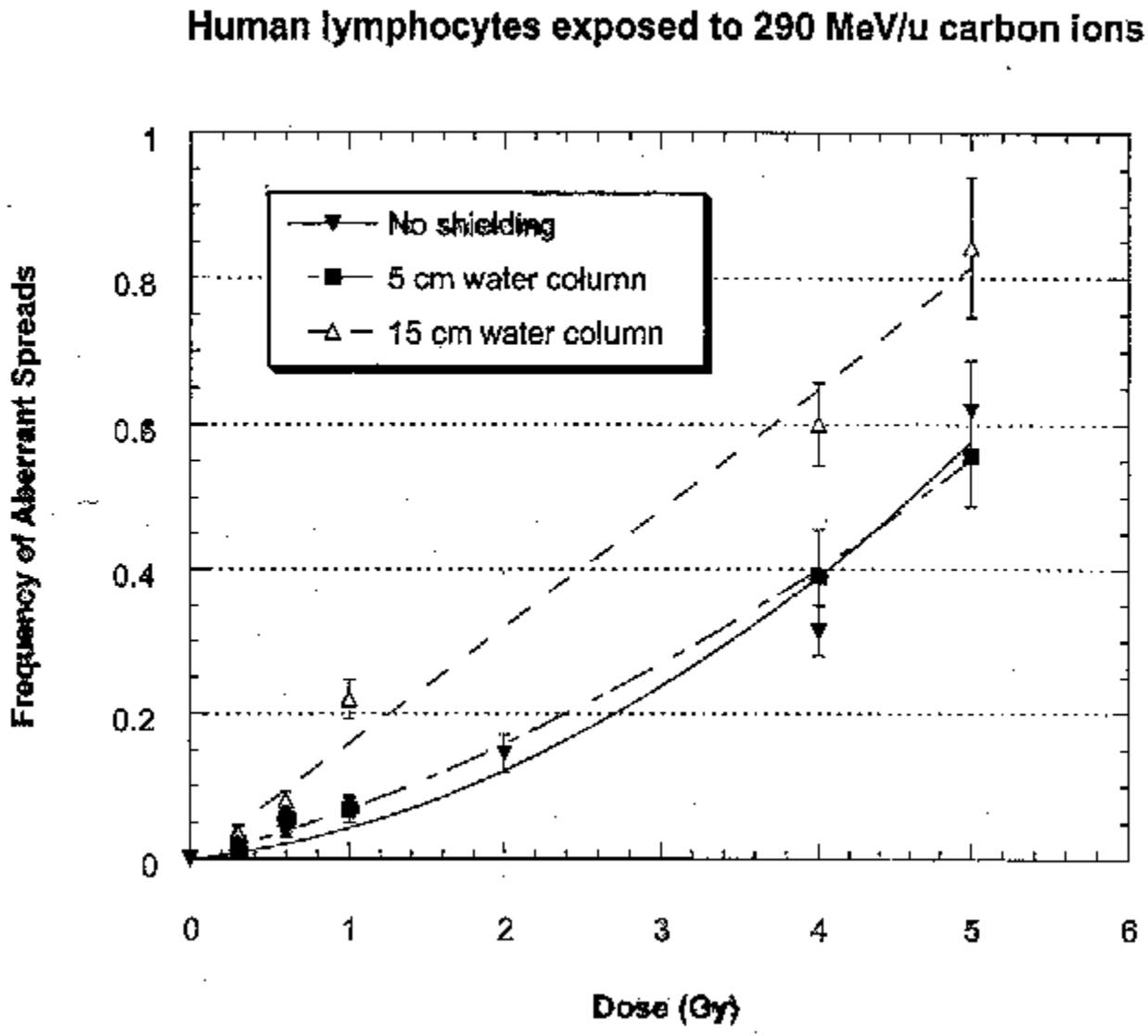
AG1522 Human Fibroblasts, Gamma-rays, Chromosome 4




AG1522 human fibroblasts
Frequency of Aberrant Cells
0.3
0.2
0.1
0.0
0
2
4
6
8
Dose (Gy)
Abb. (31 cm) p
Abb (16 cm) p (250 MeV)
Abb γ-ray
Abberant Fe (1 GeV)


Human Lymphocyte
1 GeV/u Fe
10 GeVu Au
Gamma
Total Exchanges per Cell
Dose (Gy)
0
0.5
1
1.5
2
2.5
3
3.5
4
0
1
2
3
4
5


Aberrations in chromosome # 4 of human fibroblast cells
1 GeV Fe Ion
Gamma
250 MeV Proton
Complex aberrations/cell
0.03
0.025
0.02
0.015
0.01
0.005
0
0
1
2
3
4
5
6
7
Dose (Gy)


Human lymphocytes exposed to 290 MeV/u carbon ions
No shielding
5 cm water column
15 cm water column
Frequency of Aberrant Spreads
Dose (Gy)
0
0.2
0.4
0.6
0.8
1
0
1
2
3
4
5
6

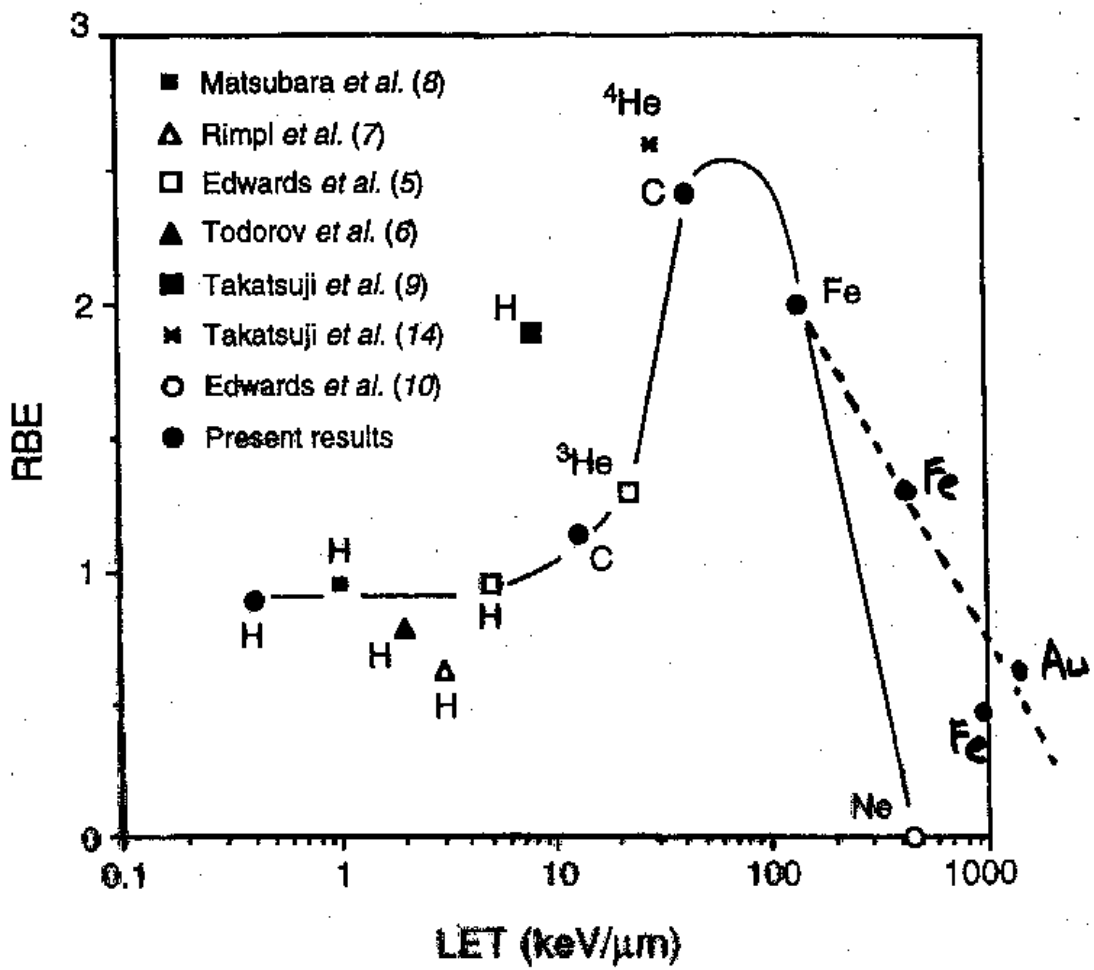
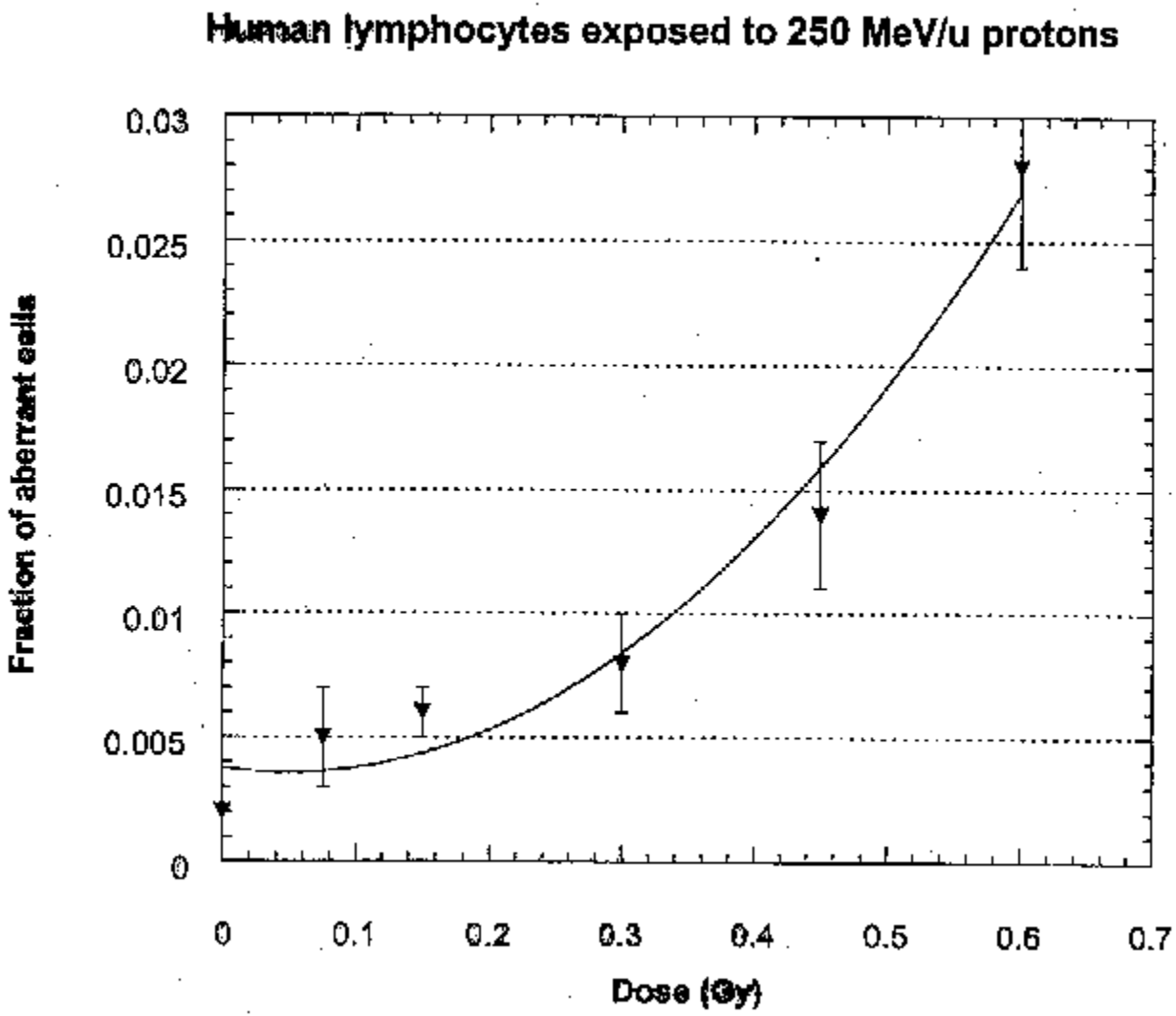


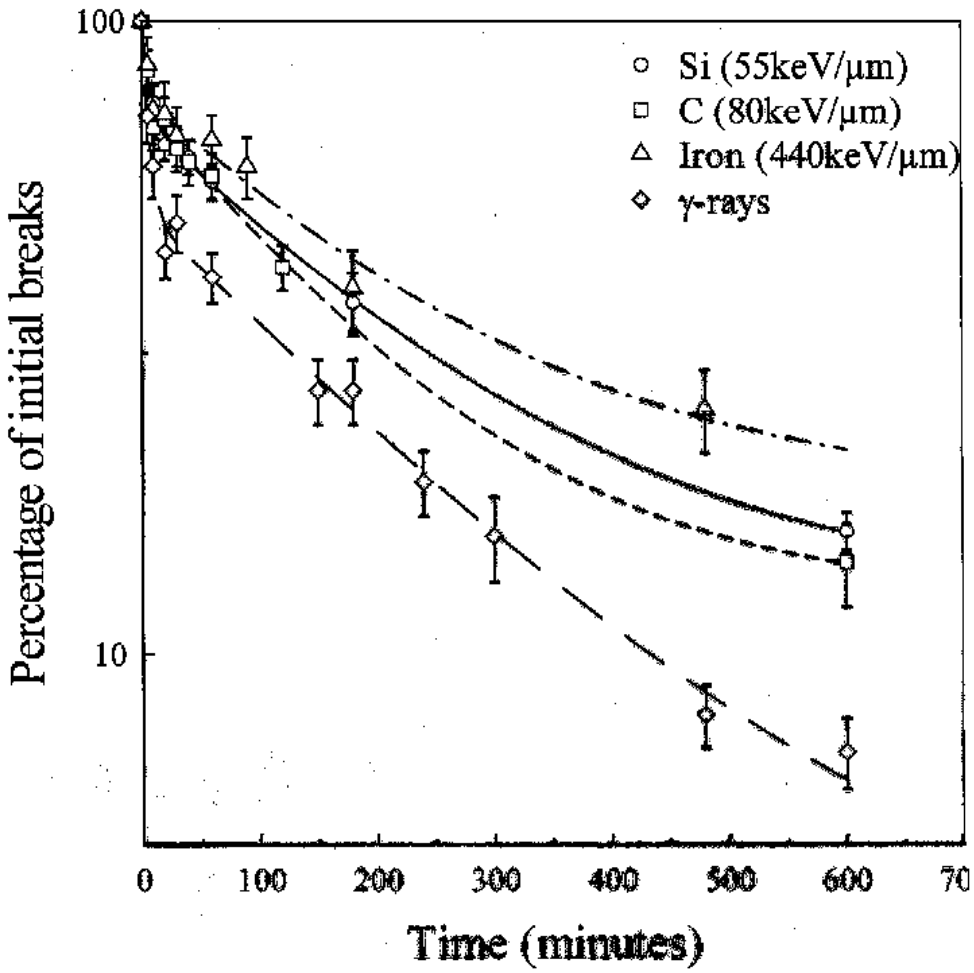
FIG. 4. RBE for interchromosome exchanges in human lymphocytes as a function LET (data fitted by eye). Interchromosome exchanges are represented by dicentrics using solid staining, and by total exchanges with the FISH technique.

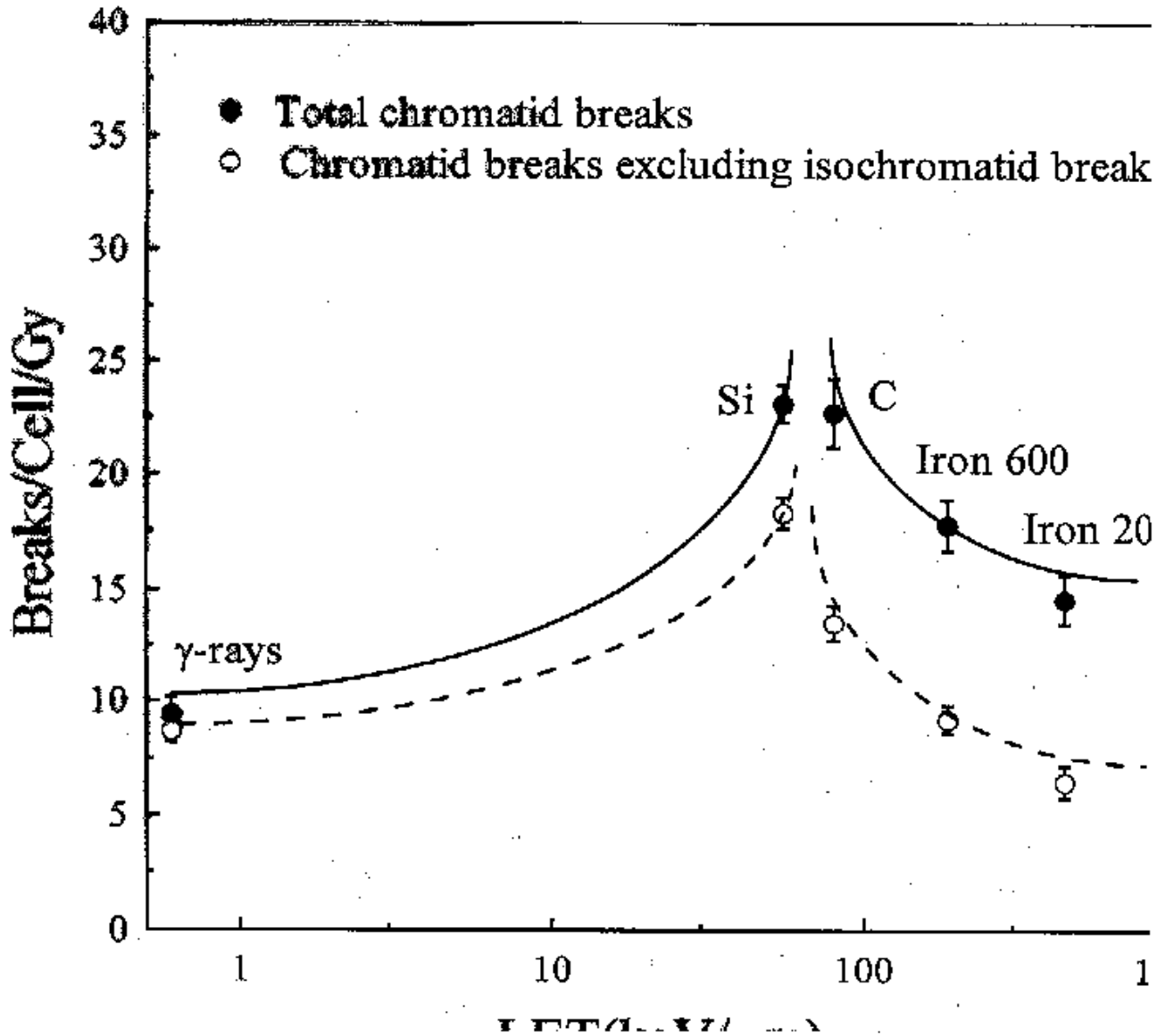
Proton experiment at Loma Linda University

- Sample: Human lymphocytes
- Energy: 250 MeV
- Dose: 7.5 – 60 cGy
- Dose rate: 7.5 cGy/hr, 30 cGy/hr, 70 cGy/min
- Shielding material: Al, 0 and 15 g/cm^2
- Harvest method: Chemical-induced PCC
- Analysis:
  Chromosomes #1 (orange), #2 (green) and #5 (yellow)


Human lymphocytes exposed to 250 MeV/u protons
Fraction of aberrant cells
0.03
0.025
0.02
0.015
0.01
0.005
0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
Dose (Gy)

Kinetics of rejoining of chromatid breaks in G2 cells




Total chromatid breaks
Chromatid breaks excluding isochromatid break
Breaks/Cell/Gy
40
35
30
25
20
15
10
5
0
Si
C
Iron 600
Iron 20
γ-rays
1
10
100
1

Initial Breaks (breaks/Gy)

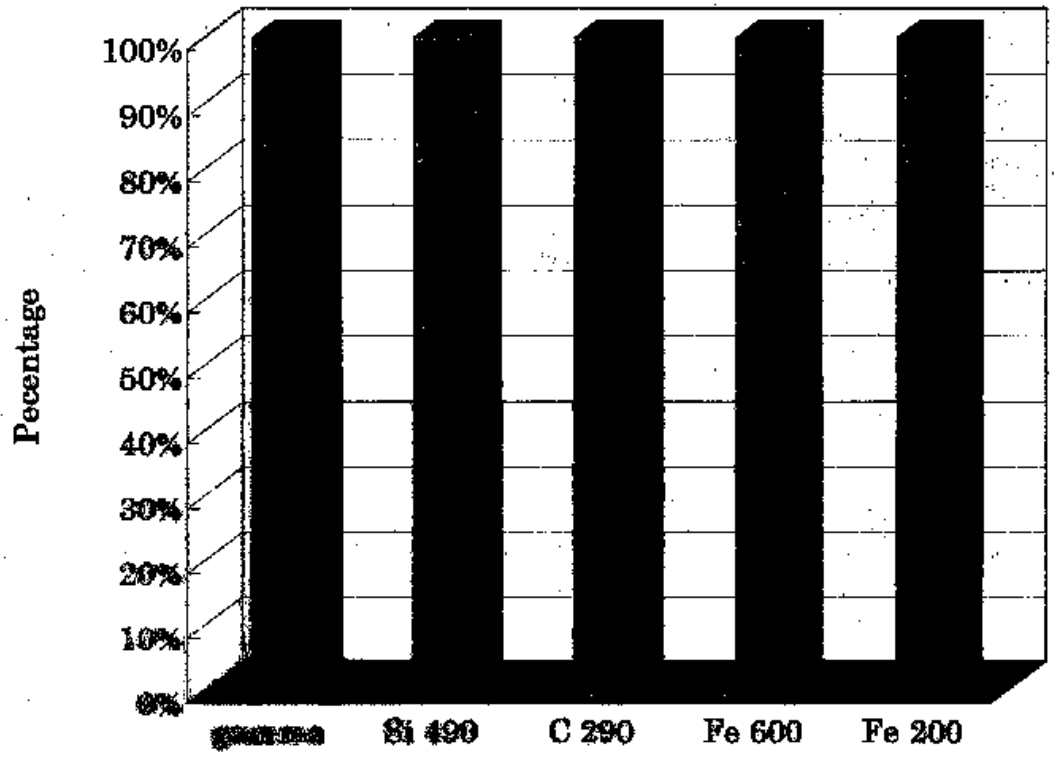


Fig 3b

The percentage of isochromatid and chromatid breaks immediately after irradiation. As LET increased, the frequencies of isochromatid breaks also increased.

Future research

- Low dose and low dose rate effects
- Effects of secondary neutrons and other secondary particles
- Biosignature of radiation quality