Effect on Testicular Development in Rats by Differences in Timing of γ-ray Irradiation

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We have no COI regarding this presentation.

Objective

Radiation is likely to affect **male reproductive organs**, and fetuses and children are more susceptible. **Azoospermia and Delayed puberty** in humans are currently a problem, there are many causes, and fetal and childhood influences may be one of them. This study investigated how irradiation at fetal, neonatal, weaning, and early sexual maturation periods affect the testicular development until adulthood.

Materials and Methods

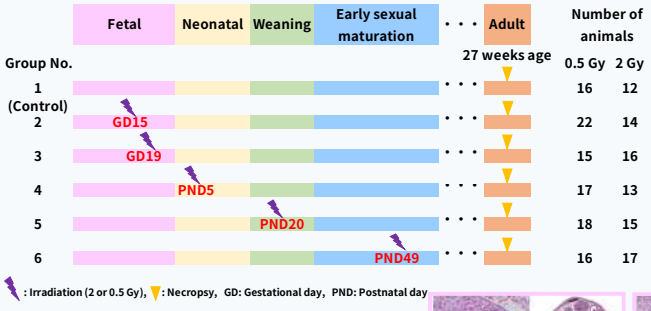
All experimental protocols involving rats in this study were reviewed and approved by the Institutional Animal Care and Use Committee of the National Institute of Radiological Sciences (NIRS) and were performed in strict accordance with the NIRS Guide for Care and Use of Laboratory Animals.

Animals: F1 hybrids of male Eker rats and female Fischer-344 (F344) rats (CLEA Japan)

Mating: Pro-estrous or estrous females were placed with an individually housed male overnight. Pregnancies were dated from gestational day 0 (GD0), being the day after mating.

Radiation exposure: Pregnant F344 rats, at **GD15** and **GD19**, and F1 rats, on **postnatal day 5 (PND5)**, **PND20**, and **PND49**, were whole-body irradiated with **0.5 or 2 Gy** of ^{137}Cs gamma irradiation at the dose rate of 0.7 Gy/min. Exposure was conducted using a Gammacell 40 (Atomic Energy of Canada). The F1 rats not irradiated with γ-rays, were set up as control animals.

Experimental protocol is as follows.

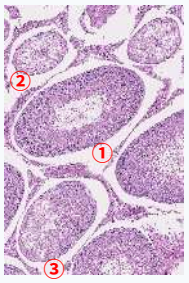


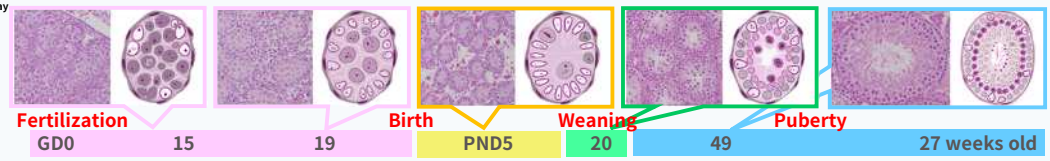
Histopathological examination: The **testis** was removed and prepared the histopathological specimens in accordance with the prescribed method. The total number of tubules in a central transverse section was counted. Moreover, the number of tubules in the three types was counted and compared for each dose and timing of γ-ray Irradiation. Tubular lesions were divided into below.

① Normal tubules

② Sertori cell-only tubules (**S-onlyTs**; absence of all germ cells)

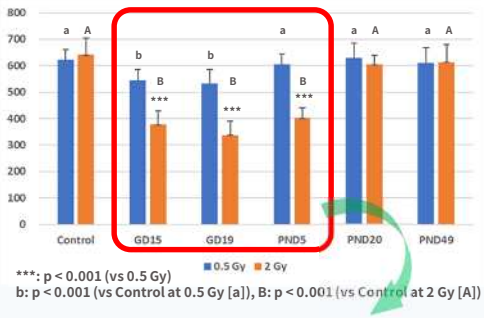
③ Partial Sertori cell tubules (**PSTs**; partial absence of all germ cells)





Results and Discussion

< Total number of tubules / one cross section>



***: p < 0.001 (vs 0.5 Gy)
b: p < 0.001 (vs Control at 0.5 Gy [a]), B: p < 0.001 (vs Control at 2 Gy [A])

It is reported that the Sertoli cell population increases from GD 13.5 until PND 15 to 20. The number of Sertori cell tubules was lower at 2 Gy than at 0.5 Gy. => Elongation of testis cord

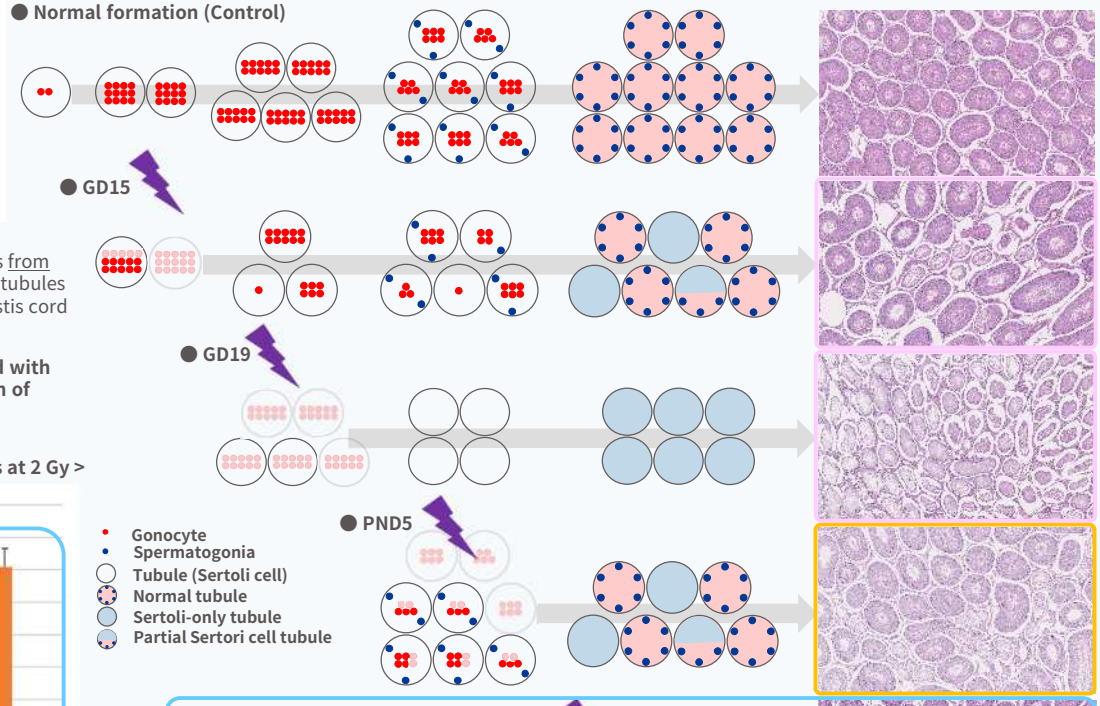
=> formation of convoluted seminiferous tubules

It was found that when Sertoli cells were irradiated with γ-ray at the time they were dividing, the elongation of the seminiferous tubules was inhibited.

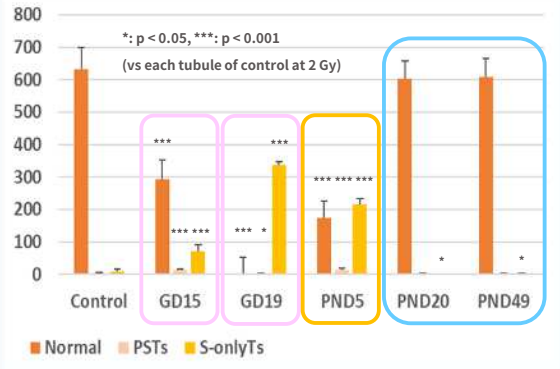
Sertoli cells: Proliferative activity↑ peak↑↑ undivided→

Gonocytes: Proliferation activity↑ undivided GST (Proliferation activity↑)

GST: Gonocytes-to-spermatogonia transition



< Each number of normal tubule, S-onlyTs, and PSTs at 2 Gy >



GD15: The gonocyte is in the process of dividing; however, the division resumes after the irradiation.

=> Not only PSTs and S-onlyTs, but also normal tubules are also noted.

GD19: During the stopping of the gonocyte dividing, a sensitive to irradiation is high, and the gonocyte are lost by apoptosis. Methylation did not occur propery.

=> S-onlyTs comprises the majority.

PND 5: The gonocyte differentiates into spermatogonia after PND 4; however, not all gonocytes finish differentiating immediately.

The first division of spermatogonia gives rise to undifferentiated spermatogonia and differentiating spermatogonia.The former remain as stem cells, while the latter progress to spermatogenesis. γ-ray Irradiation is thought to damage the cells that progress to spermatogenesis including differentiating spermatogonia, but **the undifferentiated spermatogonia (stem cells) then divide and become differentiating spermatogonia, and spermatogenesis resumes.** => **Normal tubules** are occupied in the testis.