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Radiation Induced Lung Damage: Mechanisms and Clinical Implications

Radiation therapy is one of most important therapeutic modalities for thoracic malignancies. However, radiation-induced lung damage, such as radiation pneumonitis or fibrosis, is a main dose-limiting factor when irradiating the thorax. The radiation over threshold dose results in damage to pneumocytes and endothelial cells and the inflammatory changes following the damage lead to necrosis of damaged tissue, which are then replaced by fibrotic tissue. There is diffuse lung damage and edema on histopathologic inspection; however, the tissue damage and edema is not specific for radiation injury and we are far from a reliable pathogenic model. Many parameters have been evaluated for predicting radiation pneumonitis and the most consistent predictor is cumulative radiation dose to normal lung tissue. The combination of chemotherapy probably increases the incidence and severity of radiation pneumonitis; however, this is not clear. Efforts to reduce the radiation dose to normal lung tissue using new radiotherapy techniques can reduce the incidence and severity of radiation-induced lung damage. Many biological agents have been tried to prevent and treat radiation pneumonitis; however, more data is needed. **(J Lung Cancer 2008;7(1):9 − 18)**

Key Words: Lung cancer, Radiotherapy, Radiation pneumonitis, Radiation fibrosis

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(radiation pneumonitis) ,
(radiation induced pulmonary fibrosis) , .

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(threshold radiation dose)

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(5), ,

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. (in-field radiation pneumonitis)

, (out-of-field

, , radiation pneumonitis) ,

. (classical

radiation pneumonitis) ,

(sporadic radiation pneumonitis)

. Morgan Beit

12 , 6 (8),

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, (9). Fig. 1

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. (10).

3 (3-D conformal radi-

(6). ation therapy), (intensity modulated radiation

, therapy)

50 90% 2

(7).

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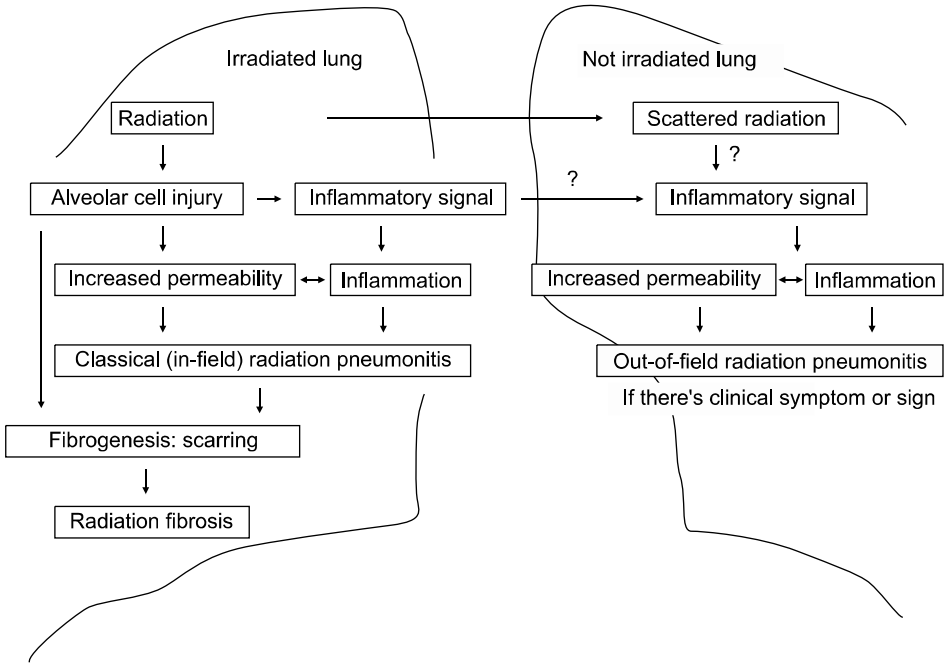

Fig. 1. Schematic mechanism of radiation pneumonitis.

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(11).

10 20% (21).

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(10).

, (22),

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(10). (23).

RTOG (Radiation Therapy Oncology Group)

NCI-CTC (National Cancer Institute-Common Toxicity Criteria) , RTOG

, , ,

. prednisolone

30 60 mg/day 1 mg/kg/day

NCI-CTC ,

(12,13). . (out-of-field radiation

(6). pneumonitis) ,

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FEV1 (forced expiratory volume in 1 second), FVC (forced vital capacity), DLCO (carbon monoxide diffusing capacity)

(24),

, 50%

. (25).

DLCO FEV1 cisplatin, paclitaxel, gemcitabine

(14,15). (17,26 29),

(6). 6 (30 32).

(16). (29),

(32).

, paclitaxel

35% (18).

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(10).

12

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, I, III, IV

, (fibronectin) (34

(8). 37).

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. (Fig. 2)

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1 (38).

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2 6 (39).

(11,33). 1

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, , (11).

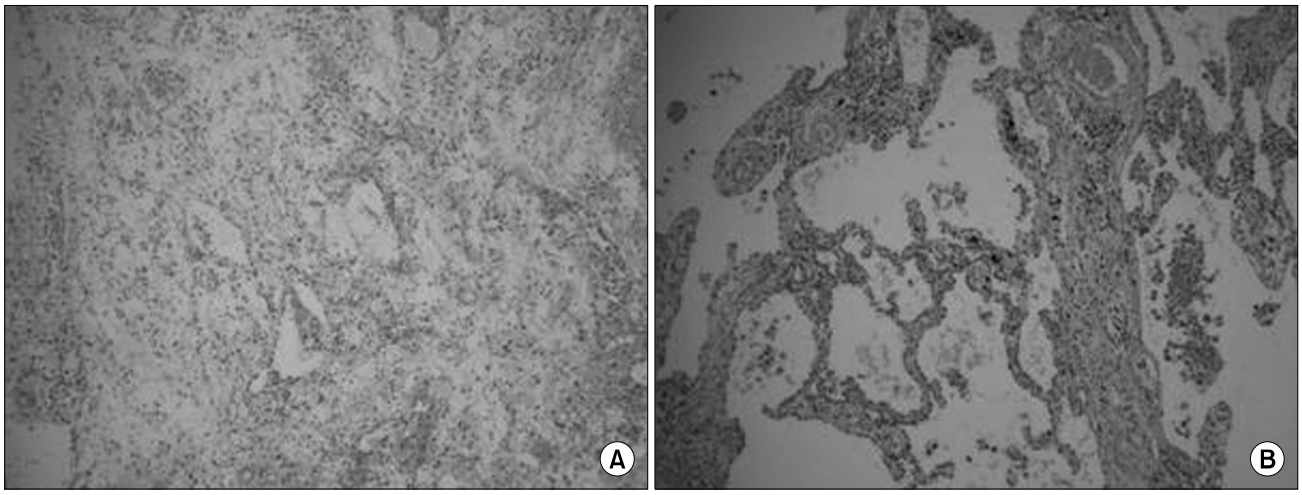

Fig. 2. Histopatholgic findings of radiation-induced lung damage. Histopathologic findings 7 weeks after 54 Gy of radiation. (A) Diffuse alveolar damage and edema, (B) Pneumocyte proliferation after radiation damage.

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(40 43).
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TGF- β
(44 51). TGF- β
, TGF- β
,
(52 54).

b-FGF, TNF- α , IL-1, IL-6, HIF (hypoxia inducing factor), PDGF, ICAM, i-NOS
(34,35,37,55 61). ,
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, (dose-volume histogram, DVH), TGF-beta (2),
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%
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V_{dose}

(mean lung dose, MLD)
(62 66), 3
V20 (20 Gy
%) 18% , V30 (30 Gy
%) 13% , V40 (40 Gy
%) 10%
(65).
Kim (66) 3

, V20, V30, V40, V50, NTCP (normal tissue complication probability) ,

. Lee (67)
3
29%
, NTCP
. NTCP S
(68,69). NTCP
(67,70),

NTCP
, ,
.

TGF- β 1 ,
(47,71).
TGF- β 1
(72,73),
TGF- β 1 .
IL-6
(74).

.

1.8 2
Gy

(conventional fractionation) 2

(accelerated hyperfractionation) .

, . CHART (continuous hyperfractionated accelerated radiation therapy)

, , CHART (75).

, .

3

, 2 0 37% (6). 3

2 37% (76) ,

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3

3

(77).

(78).

, (79,80).

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,

,

(81).

ami-fostine . Ami-fostine (aminothiol) , (82 84). 3 (85). Captopril (thiol) ACE (angiotensin converting enzyme) , (86).

TGF- β (87), Pentoxyfillin Smad TGF- β (88).

TGF- β .

ICAM-1 (89).

superoxide dismutase ROS (reactive oxygen species) , (90) (91).

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