Toho Journal of Medicine Vol.2 No.2 掲載論文の紹介

Dose distribution evaluation of internal target volume in stereotactic body radiotherapy for lung cancer
Shimizu Y, Saotome N, Futaguchi M, Kumagai S, Terahara A
Toho J Med 2（2）: 33―44, 2016

要約：

Background: Three-dimensional computed tomography (3DCT) is used in planning stereotactic body radiotherapy (SBRT) for lung cancer (3D plan). To accurately evaluate dose distribution for internal target volume (ITV), we recalculated a 3D plan using all breathing phases for four-dimensional computed tomography (4DCT).

Methods: The study included 8 patients with one tumor each who underwent SBRT for stage I lung cancer. After performing free-breathing 3DCT, 4DCT was performed. The prescription dose in the 3D plan was 48 Gy/4 fr or 56 Gy/7 fr for the ITV mean in 3DCT. We recalculated 3D plan radiation conditions for each breathing phase of 4DCT and accumulated dose distributions for all breathing phases (4D plan) with deformable image registration. A dose-volume histogram and a dose distribution map were used to evaluate dose distribution.

Results: For all patients, the maximum difference between the 3D and 4D plans for the minimum dose applied to 2% of the ITV or ITV mean was 2.6% and 1.7% respectively. For the 3 patients who exhibited substantial respiratory movement of the tumor, the dose distribution changed in accordance with the observed differences in tumor shadows for registered 4DCT and primary 3DCT during dose accumulation, and the difference between plans for the minimum dose applied to 98% of the ITV was relatively large, −6.7% to 2.9%.

Conclusions: We used 4D plan evaluation to confirm that the intended doses were applied to the ITV using the 3D plan. When using a 4D plan with deformable image registration to evaluate the dose distribution of a 3D plan, the selection of primary computed tomography for dose accumulation is important.

KEYWORDS: stereotactic body radiotherapy, stage I lung cancer, internal target volume, four-dimensional computed tomography (4DCT), deformable image registration

---

Effects of fractionated radiation on murine glioma stem cell metabolism
Fujita S, Osuka S, Shibao S, Igarashi K, Soga T, Sampetrean O
Toho J Med 2（2）: 45―52, 2016

要約：

Background: Glioma stem cells (GSCs) have an important role in tumor recurrence after treatment. We recently showed that, in a mouse model of glioma, GSCs adapt to repeated radiation exposures by changing their secretory profile and modulating survival signaling. Irradiated GSCs also reduce their rate of proliferation. In the present study we examined whether these changes require a specific adaptation of GSC energy metabolism.

Methods: Initial tumors were established in mice by orthotopic implantation of *Ink4a/Arf*-null neural stem cells transduced with human $HRAS^{V12}$. GSCs isolated from the tumors were exposed (or not) to fractionated radiation (12 fractions of 5 Gy), and five clones in each group of cells were assessed for glucose consumption, lactate production, and content of intracellular metabolites.

Results: Rates of glucose consumption and lactate production were lower in clones exposed to radiation than in nonirradiated clones, which suggests a reduction in glycolysis. Among intracellular metabolites, the high concentrations of intermediates of glycolysis and nucleoside metabolism were reduced in irradiated clones, whereas levels of essential amino acids were largely unchanged.

Conclusions: Repeated radiation changes the metabolic preferences of GSCs, in conjunction with their slowed proliferation. Future studies should thus investigate intra- and extracellular metabolites, to identify potential diagnostic and therapeutic targets for glioma recurrence.

KEYWORDS: glioma stem cell, radiation, metabolism, glycolysis, adaptation

---

Association of repeated defibrillation with outcomes for out-of-hospital cardiac arrest associated with ventricular fibrillation
（心室細動（ventricular fibrillation：VF）を呈する院外心肺停止患者に対する至適除細動回数）

Tsubota T, Honda M, Yoshihara K, Ikeda T

Toho J Med 2（2）: 53―60, 2016

要約：

背景：Ventricular fibrillation（VF）に対する除細動成功率は時間が経つにつれて急速に低下する．除細動の解析やショック時は胸骨圧迫を中断せざるを得ず，この胸骨圧迫中断の有害性も報告されている．VF に対しての適正な除細動回数を明確にすることを目的とした．

方法：ウツタイン様式を用い，日本において 2006～2010 年までに目撃があり，初回心電図が VF で，ショックまでに要した時間が 10 分以内の心原性心肺停止患者 9865 人を対象とし心拍再開率や神経予後から適正な除細動回数を検討した．

結果：心拍再開率は 38.2%，1 カ月後 cerebral performance category（CPC）1-2 獲得率 28.5%であった．ショック回数の増加とともにショック成功率や CPC1-2 獲得率は低下した．除細動回数と心拍再開の receiver operating characteristic（ROC）曲線ではカットオフ値 1.5 回，感度 65%，特異度 54%，p＜0.001，95%信頼区間（0.61-0.63）であった．また，除細動回数と CPC1-2 獲得率の ROC 曲線ではカットオフ値 1.5 回，感度 62%，特異度 52%，p＜0.001，95%信頼区間（0.57-0.60）であった．

結語：難治性心室細動に対し除細動を繰り返すと予後不良であった．患者搬送において，除細動回数も考慮に入れる必要性が示唆された．

索引用語：除細動，心室細動，心原性心肺停止，院外

Effect of the bile acid-binding resin colestimide in refractory bile acid malabsorption in patients with chronic diarrhea

Zai H, Watanabe T, Kawagoe N, Takemoto I, Tanaka H, Kijima S, Maeda T, Miyazaki T, Urita Y, Nakajima H

Toho J Med 2（2）: 61―66, 2016

要約：

Background: Recent reports indicate that bile acid malabsorption is present in about 30% of patients with chronic diarrhea and a diagnosis of diarrhea-predominant irritable bowel syndrome (IBS-D) and that treatment with bile acid–binding resin is effective. We investigated the effects of colestimide on refractory chronic diarrhea in IBS-D.

Methods: Twenty-eight patients with refractory IBS-D or chronic diarrhea were enrolled and treated with colestimide. Fifteen had no past history of gastrointestinal surgery and 13 had undergone such surgery. Small intestinal bacterial overgrowth (SIBO) was also evaluated by lactulose breath testing in 21 patients. All patients were given 1500 mg of colestimide twice a day for 2 weeks, after which the effects of colestimide treatment were evaluated.

Results: Of the 21 patients examined for SIBO, 8 (38.1%) had a positive result. Prevalence of SIBO was not associated with past surgical history (p＝0.472). In 21 (75.0%) of the 28 patients, colestimide improved diarrhea and bowel habits (p＝0.008). The effectiveness of colestimide was not associated with past surgical history or presence of SIBO.

Conclusions: Colestimide treatment had a satisfactory effect for chronic diarrhea potentially attributable to bile acid malabsorption. The effectiveness of empirical administration of colestimide for patients with refractory chronic diarrhea and IBS-D should be assessed in a future study.

KEYWORDS: diarrhea-predominant irritable bowel syndrome (IBS-D), chronic diarrhea, bile acid malabsorption, small intestinal bacterial overgrowth, colestimide

---

Serum galectin-1 autoantibodies in patients with hepatocellular carcinoma
Shiratori F, Shimada H, Nagata M, Kubota Y, Otsuka Y, Kaneko H
Toho J Med 2（2）: 67—72, 2016

要約：

Background: Although galectin-1 expression has been investigated, the clinicopathological significance of serum galectin-1 autoantibodies has not been evaluated in patients with hepatocellular carcinoma (HCC). This study investigated the clinicopathological significance of serum galectin-1 autoantibodies in patients with HCC.

Methods: Serum samples from 117 patients with HCC and 72 healthy individuals were analyzed by using an enzyme-linked immunosorbent assay system specifically developed to detect serum galectin-1 autoantibodies. The optical density cutoff value was set at 0.162 (the mean value for the controls plus 3 standard deviation). In patients positive for serum galectin-1 autoantibodies, clinicopathological characteristics were analyzed, including tumor stage and positivity rates for the conventional tumor markers alpha-fetoprotein (AFP) and protein induced by vitamin K absence or antagonist-II (PIVKA-II).

Results: The overall positivity rate for serum galectin-1 autoantibodies was 25%, which was lower than the positivity rate of 48% for AFP and 89% for PIVKA-II. No clinicopathological characteristic was associated with serum galectin-1 autoantibodies status.

Conclusions: Serum galectin-1 autoantibodies were present in patients with HCC, and serum galectin-1 autoantibodies positivity might be associated with HCC tumor progression. Although the differences between subgroups were not statistically significant, the combination of serum galectin-1 autoantibodies and a conventional tumor marker such as AFP and PIVKA-II might improve the rate of HCC detection. (Clinical trial registration number: UMIN 000014530)

KEYWORDS: galectin-1, hepatocellular carcinoma (HCC), enzyme-linked immunosorbent assay

---