Quantitative Analysis of High Dose Radioimmunotherapy with I-131 Anti-CD20 Monoclonal Antibody (Rituximab) in Patients with Non-Hodgkin's Lymphoma

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1. Introduction

Radioimmunotherapy (RIT) is therapeutic method for treatment of patient with incurable disease. I-131 is an radioisotope widely used for both diagnositic imaging and therapy, because of simultaneous emitting both gamma- and beta-ray. Recently, RIT using I-131 anti-CD20 rituximab has been introduced as one of the promising therapeutic model to treat patient with non-Hodgkin's Lymphoma (NHL)[1]. Although dosimetric approaches of low-dose I-131 rituximab imaging have been reported, there is no study of dosimetry with high-dose imaging in patient with NHL yet. In this study, we evaluated strategy of high-dose RIT and investigated the kinetic behavior and absorbed dose to bone marrow and whole body in RIT study with high-dose strategy using I-131 rituximab for NHL

2. Methods

2.1 Data Acquisition

I-131 rituximab with high-dose (5032 ~ 7400 MBq) was administrated to patients (n = 5, 19~70 yrs) with NHL. Both anterior and posterior planar images of whole body were acquired simultaneously using a gamma camera (Scintron, MiE, Germany) with high-energy collimator at 5 min, 5hr, 24hr, 48hr, 72hr and 1 or 2 weeks post administration (Figure 1). Prior to the administration, blank and transmission images were acquired using Co-57 sheet source, for attenuation correction, respectively. The setting of energy window was 363 keV ± 15% for I-131 and 122 keV ± 15% for Co-57, respectively. Venous blood was sampled at the same temporal points of imaging time, which was used for estimation of dose absorbed to bone marrow. The radioactivity of blood samples was measured (Wallac Wizard, US) after 3~4 weeks, to prevent from deadtime. During the emission acquisition, several small vials filled with known activities of I-131 were placed beside patient, for correction of deadtime due to high-activity of I-131.

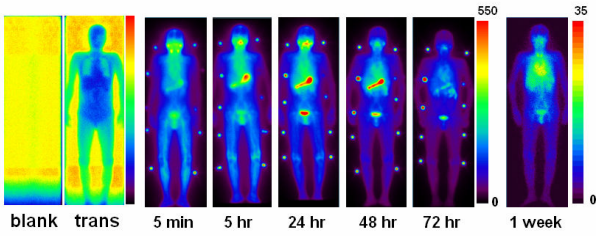

Figure 1. Sequential images of I-131 rituximab after injection, according to the protocol described in the above section (2.1 Data Acquisition). Before the injection of I-131 rituximab, both blank and transmission scan were performed using Co57 planar source, and serial emission scans were acquired with time.

2.2 Estimation of Absorbed Dose

The acquired anterior and posterior images were converted to geometric mean image for further analysis. From the sequential images with corrections of deadtime and photon attenuation, time-activity curve (TACs) of whole-body activities was obtained. Using the TACs of blood and whole body, the values of effect half-life of the blood and whole body time-activity curves were calculated respectively. In the estimation of effect half-life, bi-exponential function was used in curve fitting process. The cumulated activity and residence time of both TACS were calculated, and the values of patient specific absorbed doses to bone marrow and whole body were estimated by means of the approaches suggested by Sgourous[2] and Wahl[3], respectively. The amount of dose contribution organ was evaluated by using a program of MIRDOSE[4].

3. Results

Deadtime on gamma images induced underestimation (~64%) of area under the TAC of whole body radioactivity (Figure 2). The radioactivity in blood and whole body decreased rapidly with time, and the residence time of blood, bone marrow and whole body were 27.5 ± 6.7 hr, 0.82 ± 0.43 hr and 27. 2 ± 13.5 hr, respectively..The values of mean absorbed dose were range from 26.1 to 0.93.9 cGy (59.4 ± 31.9) for bone marrow and from 12.3 to 62.6 cGy (32.7 ± 20.1) for whole body, respectively. The dominant contribution of dose was from bone marrow self dose (> 60%) (Table 1).

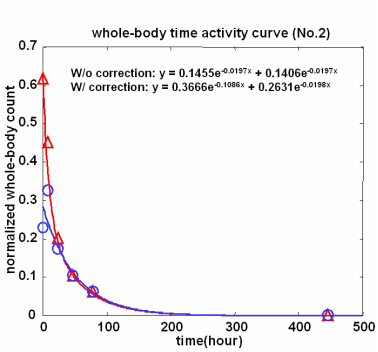

Figure 2. The effect of deadtime on whole body count used in whole body estimation. Deadtime effect due to high activity induced significant underestimation of activity, in special, in the early part of time-activity curve, which resulted in underestimation of absorbed dose.

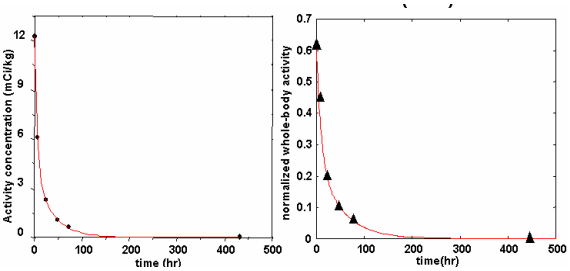

Figure 3. Typical types of time activity curves of blood (left) and whole body (right) activities.

No.	Injected dose (mCi)	Body Weight (kg)	Residence time estimated (hour)		Radiation Dose estimated (cGy)		Primary contribution (percentage%)	
			BM	WB	BM	WB	BM	WB
1	136	70.0	0.33	12.86	26.1	12.3	BM (62.3)	RB (97.5)
2	185	65.6	0.44	14.06	37.2	16.0	BM (66.8)	RB (97.0)
3	200	60.0	0.95	28.81	92.9	38.8	BM (68.0)	RB (96.8)
4	156	74.2	1.07	38.4	46.8	33.9	BM (64.2)	RB (97.3)
5	263	72.2	1.33	42.1	93.9	62.6	BM (67.0)	RB (96.9)

Table 1. Summarized results of estimated values of residence time and absorbed dose of bone-marrow and whole-body, respectively. In the table, BM, WB, and RB mean bone-marrow, whole body, and remained body, respectively.

4. Conclusion

Using the RIT protocol with high-dose I-131 rituxmab, quantitative estimation of absorbed dose to bone marrow and whole body was possible. This RIT strategy of I-131 rituxmab would be useful in monitoring treatment for NHL.

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