EVALUATION OF THE TREATMENT OUTCOME OF LYMPHOMA PATIENTS AFTER THE FIRST TREATMENT USING MAGNETIC RESONANCE IMAGING BASED VOLUMETRY.

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Abstract: The aim of this study was to evaluate the treatment outcome of non-Hodgkin lymphoma patients measured as tumour volume change after the first treatment of chemotherapy using magnetic resonance based volumetry. The study material consisted of nineteen non-Hodgkin lymphoma patients. Semiautomatic segmentation software Anatomatic™ and a region growing technique was used for the analysis. The average volume of the tumours before the treatment was 537 cm^3 (range 72 - 2144 cm^3). The average volume of the tumours after treatment was 362 cm^3 (range 30 - 1622 cm^3). In all patients the tumour volume decreased with the average decline in volume being 167 cm^3. The average decline in tumour volume was 41% (range 3% - 76%). The average intraobserver variation was 7.7%, interobserver 10.6%. Promising results were achieved based on the estimations of tumour volume before and after the treatment. The software was suitable for the task.

Introduction

Lymphoma represents a diverse spectrum of malignant neoplasms of the lymphoid system. It is broadly categorized into Hodgkin's lymphoma and non-Hodgkin's lymphoma. The differences are in the histological characteristics and dissemination [8, 17]. CT is the primary imaging modality in detection and visualization of lymphomas, supplemented by ultrasonography and magnetic resonance imaging [8]. Magnetic resonance imaging is important in assessing central nervous system diseases and providing additional information in problematic areas. [8].

Many studies have been reported assessing the reliability and reproducibility of estimating volumes of anatomical regions based on radiological modalities using semiautomatic methods. The semiautomatic region growing and isocontour algorithms have previously shown to have the potential to be used in determining tumour volumes [14]. In liver segmentation a semiautomatic segmentation algorithm is substantially more accurate and less time consuming than a manual method in volumetric measurements of liver segments [12]. The region-growing technique has been used to generate accurate and reproducible segmentation of prostate, bladder and rectum from CT data [15]. The semiautomatic seed growing and region deformation methods have produced satisfactory results in estimating tongue carcinoma volumes from MRI images [2]. Satisfactory results were achieved in estimating nasopharyngeal carcinoma volumes using MRI based semiautomatic segmentation [18]. Semiautomatic segmentation is a rapid and reproducible method in estimating volumes of ovarian tumours [7]. However, not many studies have been done about using semiautomatic segmentation to estimate tumour volumes in non-Hodgkin lymphomas.

The ability to produce reliable and reproducible estimations of non-Hodgkin lymphoma volumes and measuring change in tumour volumes is important because it presents a possibility to evaluate the treatment outcome of non-Hodgkin lymphoma patients with a new, reliable and fast method.

The aim of this study was to evaluate the treatment outcome of non-Hodgkin lymphoma patients after the first treatment of chemotherapy. using magnetic resonance imaging based volumetry. For this aim we used the semiautomatic segmentation software Anatomatic™ [10]. It has been used before with success to estimate volumes of anatomical regions, brain lesions and ovarian tumours [3, 4, 6, 7, 11]. This is a unique study involving accurate volumetric estimation of non-Hodgkin lymphoma tumours of the abdominal and thoracic regions.

This study is a part of a more comprehensive research project which will evaluate the treatment outcome of the whole treatment process using magnetic resonance imaging (MRI), computed tomography (CT) and positron emission tomography (PET) based volumetry.

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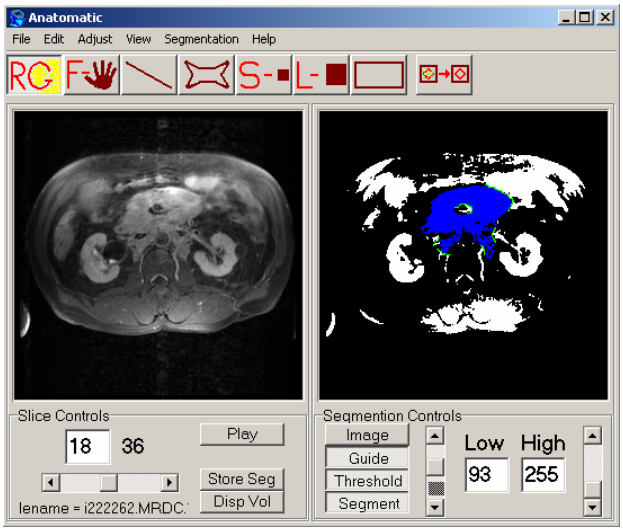

Figure 1: Anatomatic™ user interface, an unsegmented MRI image on the left, and a segmented one on the right

Materials and Methods

All together twenty two non-Hodgkin lymphoma patients were enrolled from March 2002 to August 2004 at the Department of Oncology in Tampere University Hospital in Finland. The selection criteria were as follows: age between 16-78 years, a histologically confirmed non-Hodgkin lymphoma needing chemotherapy and the minimum diameter of the biggest bulk 3cm. Physical competence had to be better than Zubrod class 4 [19]. The treatment was chemotherapy + anti-CD20 antibody rituximab.

Exclusion criteria were gravidity, psychosis, diabetes with insulin treatment, HIV-positivity, AIDS, another malignity or another serious disease which prevents chemotherapy, inability to perform initial CT- and MRI-scans within a week from each other.

One of the patients dropped out during the study, one patient passed away before the second MRI scan and one patient's second MRI scan was not found later in the image archive. So, final number of patients in the study was nineteen.

Five of the patients were women and fourteen men. Both CT- and MRI scans were performed before and after the treatment. At the time of the first MRI scan the average age of the patients was 61.9 years, (range 34 - 76 years). After the initial scan, the first treatment was administered. The second CT- and MRI-scans were conducted two weeks after the first. In 17 cases the tumour was situated in the abdominal area and in three cases in the thoracic area. Patient data is summarised in Table 1.

All patients were studied on a 1.5 tesla MRI machine (Signa, General Electric, Wisconsin). The MRI protocol included coronal T1 weighted sequence, axial fat saturated T2 weighted fast spin echo (FSE) sequence, axial fat saturated T1 weighted sequence, volumetric 3D T2 fast spin echo sequence and axial and coronal T1 weighted fat saturated sequence.

We used only the contrast enhanced axial sequences for the volumetric analysis before and after the first treatment. Images were then transferred to another computer equipped with Anatomatic™ software running on normal PC surroundings. The slice thickness ranged from 5mm to 10mm with a 0mm gap. In one patient the gap was 2mm. MRI parameters were as follows: TE=10, TR=620, FOV ranged from 34 to 46, Matrix 256x256.

Semiautomatic seqmentation software Anatomatic™ and a region growing technique was used for the volumetric analysis. Anatomatic™ user interface is illustrated in Figure 1.

For segmentation certain regions of interest (ROI) areas were determined. The cut-off points for the ROI areas were determined based on anatomical structures which limit most of the tumour burden, and only the tumour volume between these cut-off points was determined. The final volume of the tumour burden was calculated using a multiply factor from the voxel count.

Inter- and intraobserver variations were calculated. Six study patients were selected for this randomly using a third party and blindfold. Their MRI images taken before treatment were then segmented again, and these volumes were compared to the initial volume estimates. At least 8 weeks passed between the initial volume estimations and the inter- and intraobserver estimations.

The software had been calibrated earlier using a phantom with an error of only 1.5% between the actual volume of the phantom and the volumes calculated with MRI [11]. Also both inter- and intraobserver studies had been performed earlier with variation ranging from 3.5% to 7%.

Table 1: Patient data

Patient	Age (years)	Sex	Tumour location
1	68	Female	Thorax
2	61	Female	Abdomen
4	74	Male	Abdomen
5	62	Male	Abdomen
6	73	Female	Abdomen
7	63	Male	Abdomen
8	71	Male	Abdomen
9	56	Male	Abdomen
11	72	Male	Abdomen
12	48	Female	Abdomen
13	76	Male	Abdomen
14	63	Female	Abdomen
15	53	Male	Abdomen
16	56	Male	Abdomen
17	49	Male	Thorax
18	34	Male	Abdomen
19	56	Male	Abdomen
20	67	Male	Thorax
22	74	Male	Abdomen

Results

The average volume of the tumours before treatment was 537 cm^3 (range 72 - 2144 cm^3). The average volume of the tumours after treatment was 362cm^3 (range 30 - 1622 cm^3).

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After the treatment, tumour volume had decreased in all patients. The average decline in tumour volume was 41% (range 3% - 76%). Tumour volumes and changes are summarised in Table 2. The average time of segmentation of one patient was from 20 to 30 minutes. The average intraobserver variation was 7.7%. The average interobserver variation was 10.6%. Intraobserver and interobserver variations are summarised in tables 3 and 4.

Table 2: Tumour volumes and changes

Patient	Start volume (cm^3)	End volume (cm^3)	Volume change (cm^3)	Volume change (%)
1	429	105	324	76
2	183	64	119	65
4	173	66	107	62
5	529	459	70	13
6	570	419	151	26
7	800	595	205	26
8	146	118	28	19
9	118	80	38	32
11	367	246	121	33
12	850	769	81	10
13	2144	1622	522	24
14	72	30	42	58
15	140	52	88	63
16	274	93	181	66
17	795	190	605	76
18	824	797	27	3
19	750	579	171	23
20	273	66	207	76
22	771	522	249	32

Table 3: Intraobserver variation

Patient	Initial Result (cm^3)	Intraobs. Result (cm^3)	Difference (cm^3)	Variation (%)
2	183	185	2	1.1
8	146	136	10	7.4
9	118	129	11	8.5
14	72	62	10	16.1
16	274	259	15	5.8
18	824	770	54	7.0

Table 4: Interobserver variation

Patient	Initial Result (cm^3)	Interobs. Result (cm^3)	Difference (cm^3)	Variation (%)
2	183	205	22	10.7
8	146	132	14	10.6
9	118	111	7	6.3
14	72	66	6	9.1
16	274	266	8	3.0
18	824	666	158	23.7

Discussion

In this study promising results based on non-Hodgkin lymphoma volume and volume change estimations were achieved. The software Anatomatic™ was a newer, more stable version than the previous one used in other studies [10]. The region growing technique was used in the segmentation.

The time consumption was reasonable, 20 - 30 minutes per patient. In previous studies segmentation of ovarian tumours using MRI based volumetry took 15 - 20 minutes and nasal airway segmentation using CT based volumetry took 30-50 minutes [5, 7]. Using Anatomatic™, MRI based semiautomatic segmentation of cerebral infarctions took 5 to 10 minutes per patient [3]. In the present study of non-Hodgkin lymphomas however, semiautomatic segmentation could not be used all the time.

Semiautomatic segmentation was used as much as possible. The original films were not needed. However, tumour linings were in a few cases difficult to distinguish, especially next to the liver and the spleen. In those cases some manual segmentation had to be done. This is possibly one reason for the rather large average interobserver variation of 10.6% and especially the large interobserver variation concerning the tumour of patient no. 18.

In addition, in some patients the tumour tissue intensity changed after treatment to an intensity which was very close to the intensity of neighboring tissue. That proved to be an additional difficulty in the segmentation process. The changes in intensity could indicate that tumour activity and thus morphology had been changed by the treatment.

Several automatic segmentation methods have been used to estimate volumes of brain lesions and tumours [1, 9, 13]. Automatic methods however, are not very suitable techniques in determining the volumes of non-Hodgkin lymphoma tumours because the contrast between tumours and the surrounding anatomical regions is sometimes very low and tumour linings in some places are not distinct.

We did not compare the changes in the patients' clinical parameters with changes in tumour volumes. However, this study is part of a more comprehensive research project. One part of it is to use CT based volumetry to estimate non-Hodgkin lymphoma volumes and volume changes.

In the future, we intend to compare the changes in non-Hodgkin lymphoma volumes to changes in several clinical parameters and to compare MRI based volumetry to CT based volumetry. Rasch et al. [16] studied the potential impact of combined use of CT and MRI images in estimating gross tumour volumes (GTV) of head and neck cancers. It was concluded that MRI derived GTVs were smaller and had less interobserver variation than CT derived GTVs.

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Conclusions

Based on the results of this study, using MRI based volumetry to estimate volumes of non-Hodgkin lymphomas before and after the first treatment of chemotherapy, promising results were achieved. The software was suitable for the task. We intend to evaluate the whole treatment process and to compare MRI based volumetry with CT and PET based volumetry with a larger patient sample size.

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