Secondary cancers and heart diseases risk in early stage Hodgkin's lymphoma: 3D-CRT *vs* VMAT

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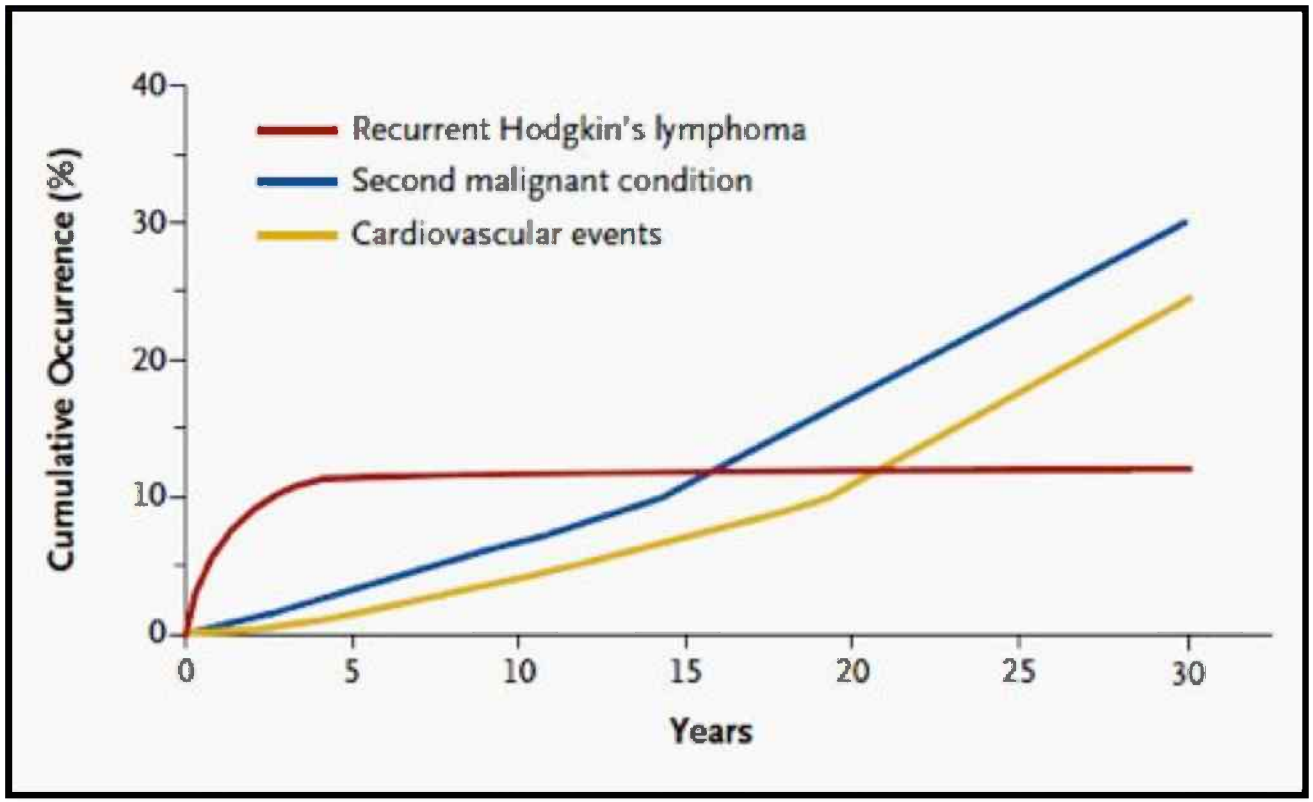
BACKGROUND



Early-Stage HL

[Armitage et al, NEJM, 2010]

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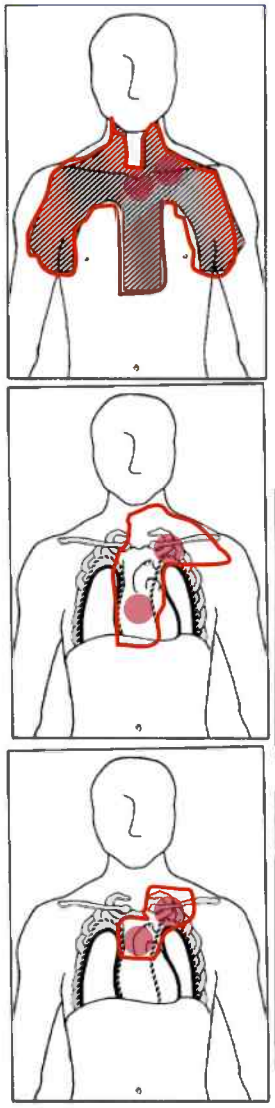

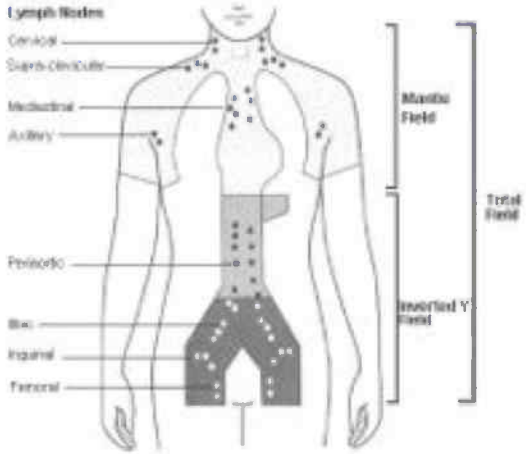

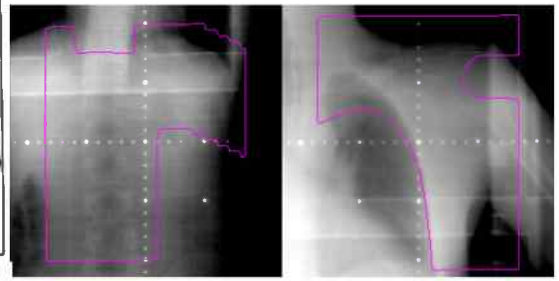

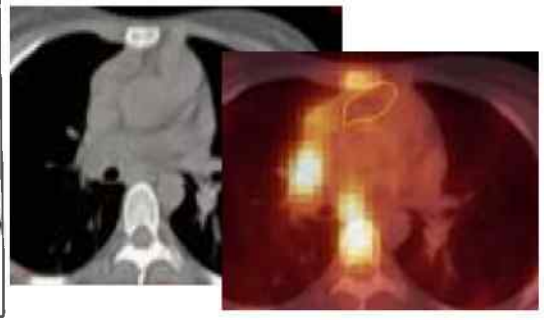

1970

Extended fields

DFT≈40 Gy

MOPP

Involved fields

DFT≈30 Gy

ABVD

Involved node / Involved site

DFT≈20 Gy

2014

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BACKGROUND

Various IMRT solutions have been implemented over the years:

→ superior target coverage and organs at risk sparing

[Goodman et al, IJROBP, 2005; Girinsky et al, IJROBP, 2006; Weber et al, IJROBP, 2009; Paumier et al, IJROBP, 2011; Koeck et al, IJROBP, 2012]

→ larger amount of thoracic tissues receiving low or very low doses with the potential increase in radiation-induced malignancies

[Hall et al, IJROBP, 2003]

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BACKGROUND

Studies based on radiobiological estimates of secondary cancers risk starting from individual patients dose-volume histograms for different IMRT techniques have been conducted in recent years

Changes in breast cancer risk associated with different volumes, doses, and techniques in female Hodgkin lymphoma patients treated with supra-diaphragmatic radiation therapy

Andrea Riccardo Filippi MD*, Riccardo Ragona PhD, Marco Fusella PhD, Angela Botticella MD, Christian Fiandra PhD, Umberto Ricardi MD

Practical Radiation Oncology (2013)

Estimated risk of cardiovascular disease and secondary cancers with modern highly conformal radiotherapy for early-stage mediastinal Hodgkin lymphoma

M. V. Maraldo[1*], N. P. Brodin[1,2], M. C. Aznar[1], I. R. Vogelius[1], P. Munck af Rosenschöld[1,2], P. M. Petersen[1,3] & L. Specht[1,3]

Annals of Oncology 24: 2113–2118, 2013

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PURPOSE

The present study has been designed with the aim of further investigating the potential risks of late toxicity (second cancers, cardiovascular diseases) associated to Butterfly-VMAT in patients treated with INRT or ISRT for stage I-IIA HL involving the mediastinum

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MATERIALS AND METHODS

Patients' selection

38 patients
(13 males and 25 females)

Stage I-IIA HL

INRT or ISRT after chemotherapy between 2008 and 2012

Disease presentation at diagnosis:

- mediastinum alone
- mediastinum plus unilateral neck involvement
- mediastinum plus bilateral neck involvement

Characteristic	*n*	%
No. of patients	38	
Age (y) Range Mean	 15 – 43 30	
Sex Male Female	 13 25	 34.2 65.8
Ann Arbor Stage I II	 8 30	 21.1 78.9
Bulky	8	21.1
EORTC prognostic groups Favorable Unfavorable	 15 23	 39.5 60.5
Involved sites Mediastinum alone Mediastinum and unilateral neck Mediastinum and bilateral neck	 8 19 11	 21.1 50 28.9

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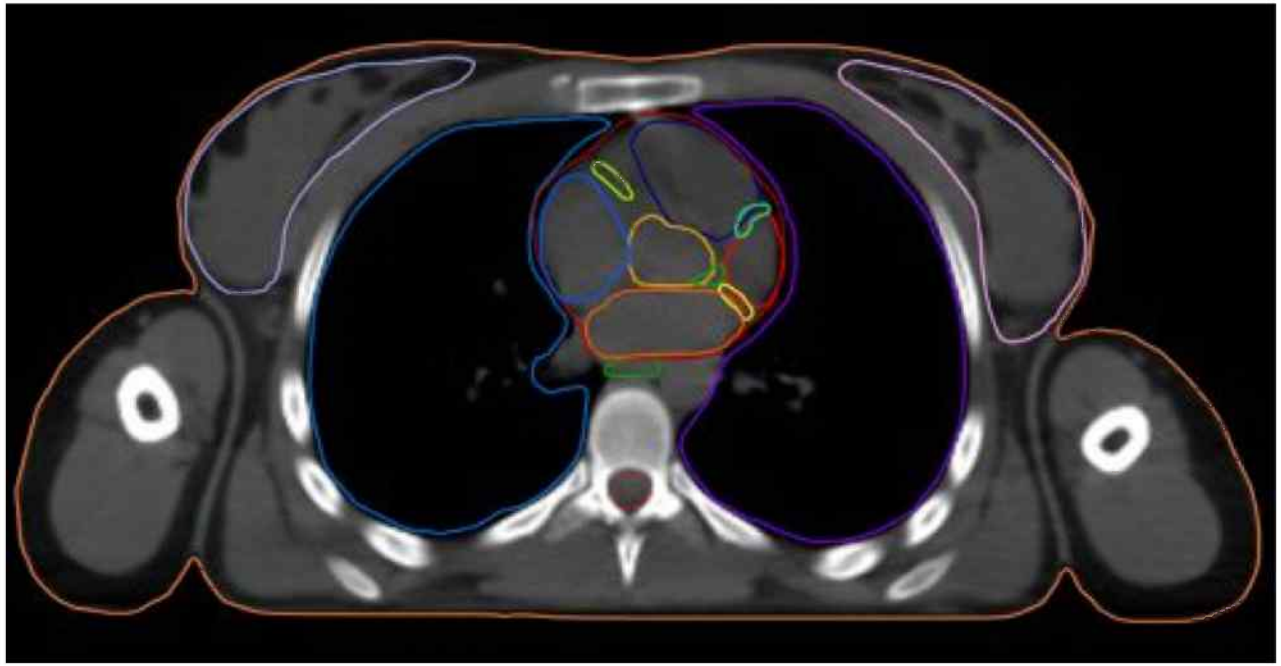
MATERIALS AND METHODS

Radiotherapy technique

CTV according to involved node or involved site guidelines

PTV = CTV + 5-mm isotropic margin

OARs: lungs, thyroid, breasts and cardiovascular structures



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MATERIALS AND METHODS

Radiotherapy technique

Structure	Parameter	Objective
PTV	D_{mean}(Gy)	30
	$V_{90\%}$ (%)	99
	$V_{95\%}$ (%)	95
	$V_{107\%}$ (%)	1
Breast	V_{4Gy} (%)	50
	V_{10Gy} (%)	33
Lung	V_{5Gy} (%)	50
	V_{10Gy} (%)	33
Thyroid	V_{18Gy} (%)	50
	V_{25Gy} (%)	33
Heart	$V_{7.7Gy}$ (%)	50
	V_{15Gy} (%)	33
Coronary Ostia	V_{20Gy} (%)	100

[Fiandra et al, Radiat Oncol, 2012]

Prescription dose:

30 Gy in 2 Gy daily fractions

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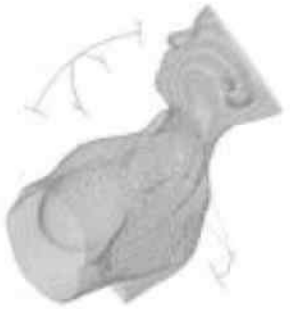
MATERIALS AND METHODS

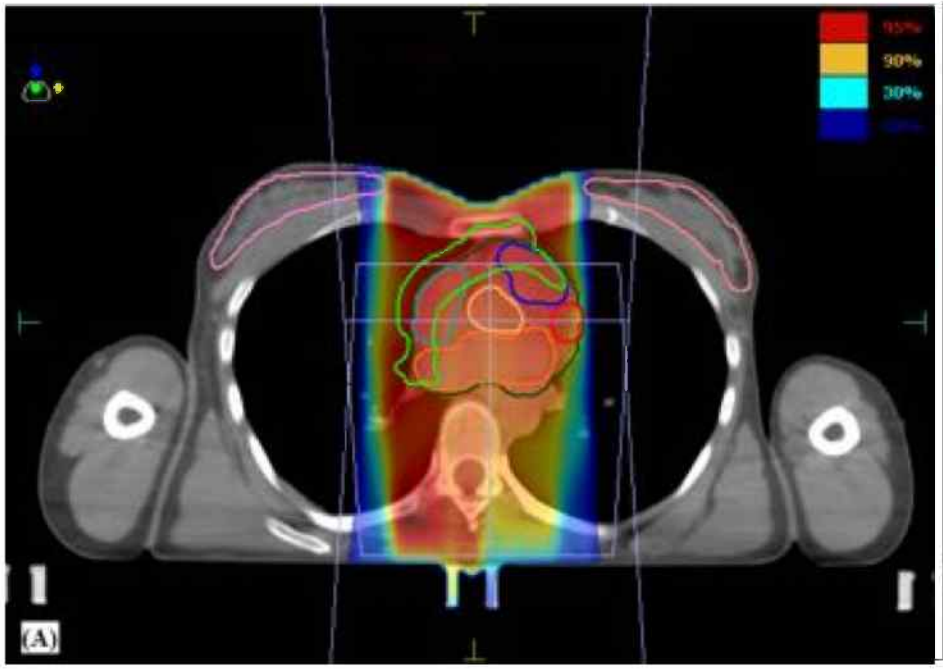
Radiotherapy technique

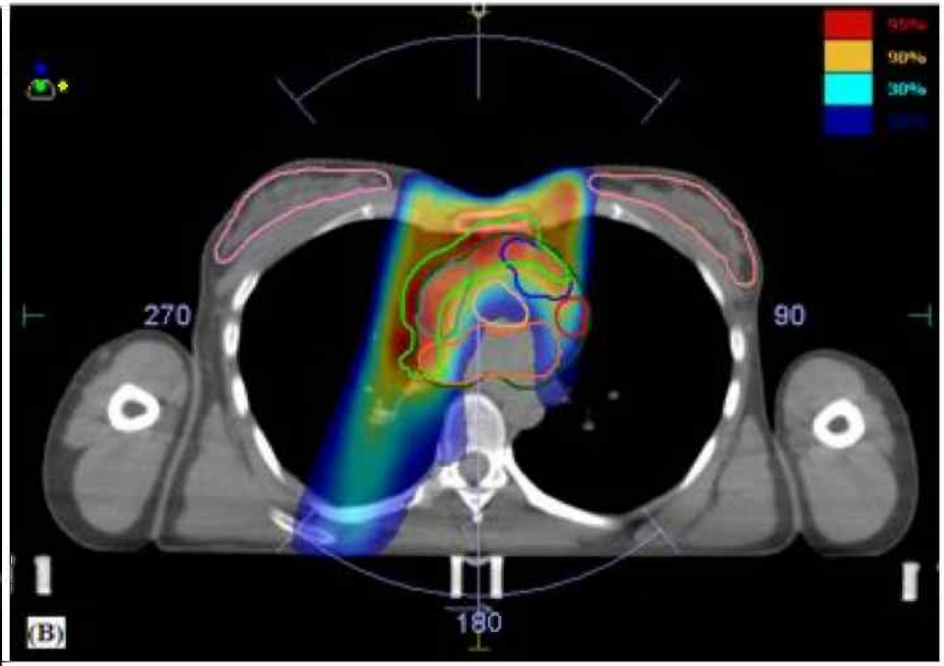


Conventional 3D-CRT plan (AP-PA)

VS

"Butterfly" VMAT (B-VMAT)





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MATERIALS AND METHODS

Risk estimation

Second cancers

Dose Volume Histogram (DVH):

→ Organ Equivalent Dose (OED) *[Schneider et al, IJROBP, 2005]*

→ Excess Absolute Risk (EAR) *[Schneider et al, Theor Biol Med Model, 2011]*

→ Lifetime attributable risk (LAR) *[Kellerer et al, Radiat Environ Biophys, 2001]*

Cardiovascular disease (CD) and valvular disease (VD)

Mean doses extracted from the DVH:

→ Absolute Excess Risk (AER) *[Maraldo et al, IJROBP, 2012]*

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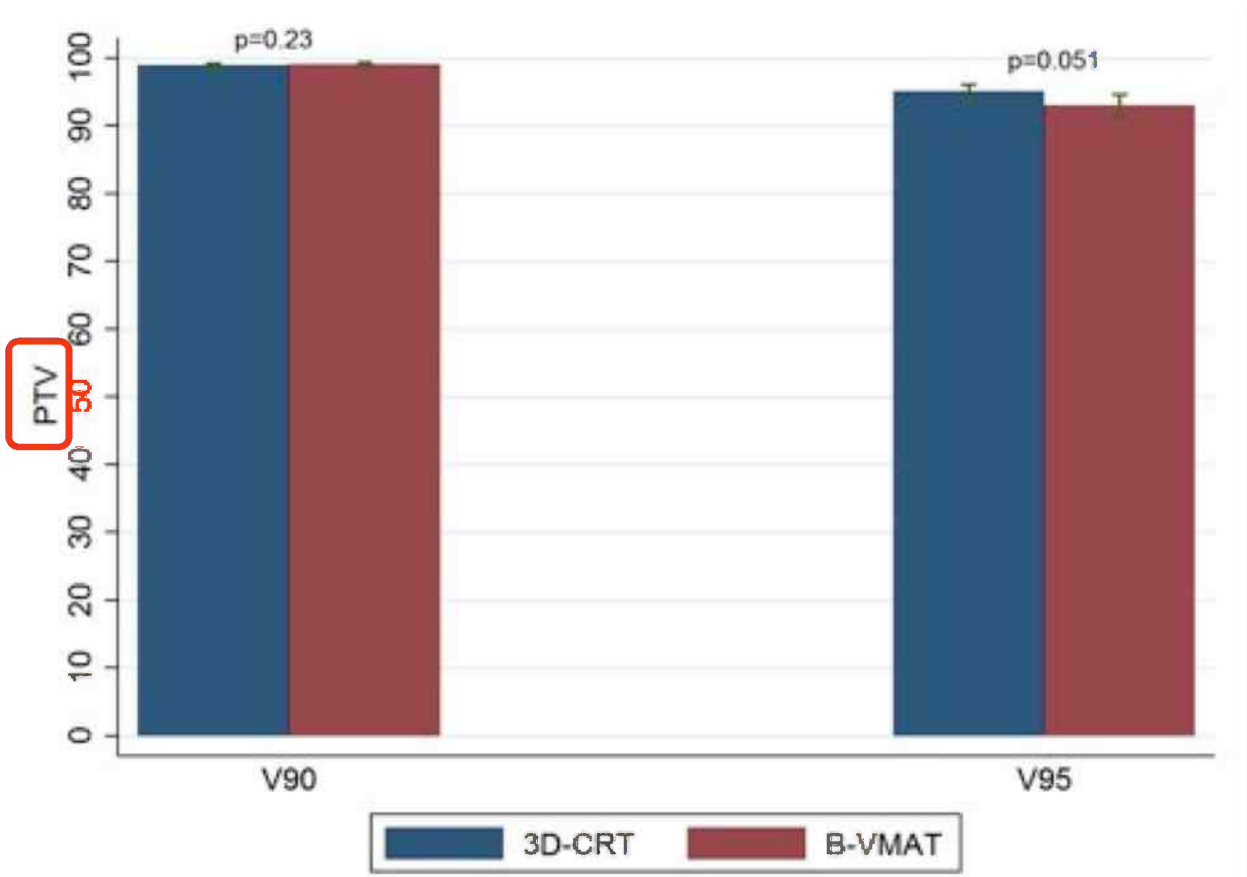
RESULTS

Dosimetric parameters



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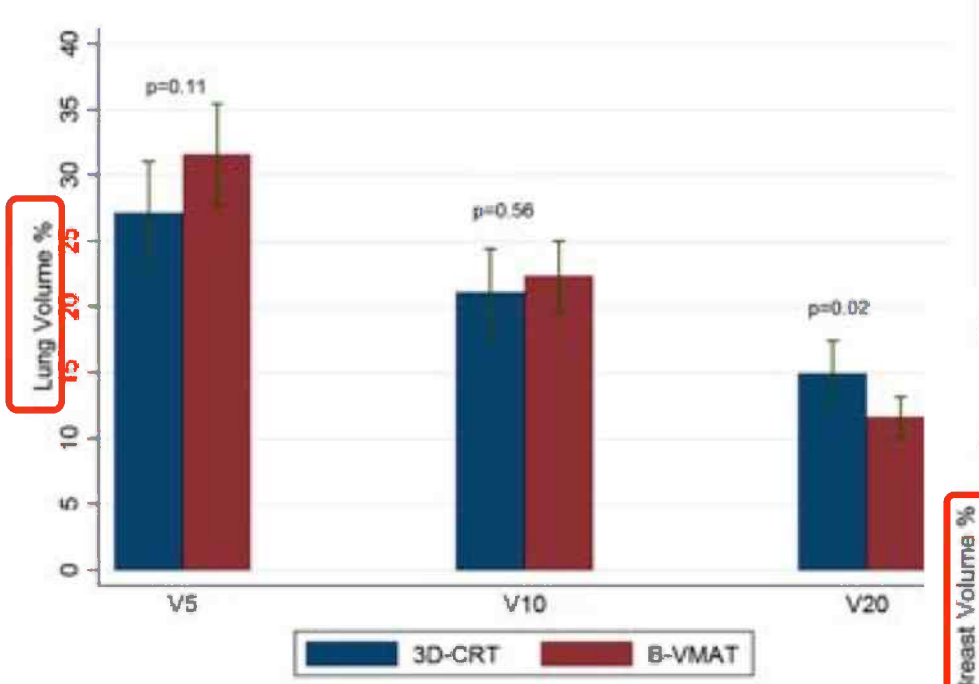
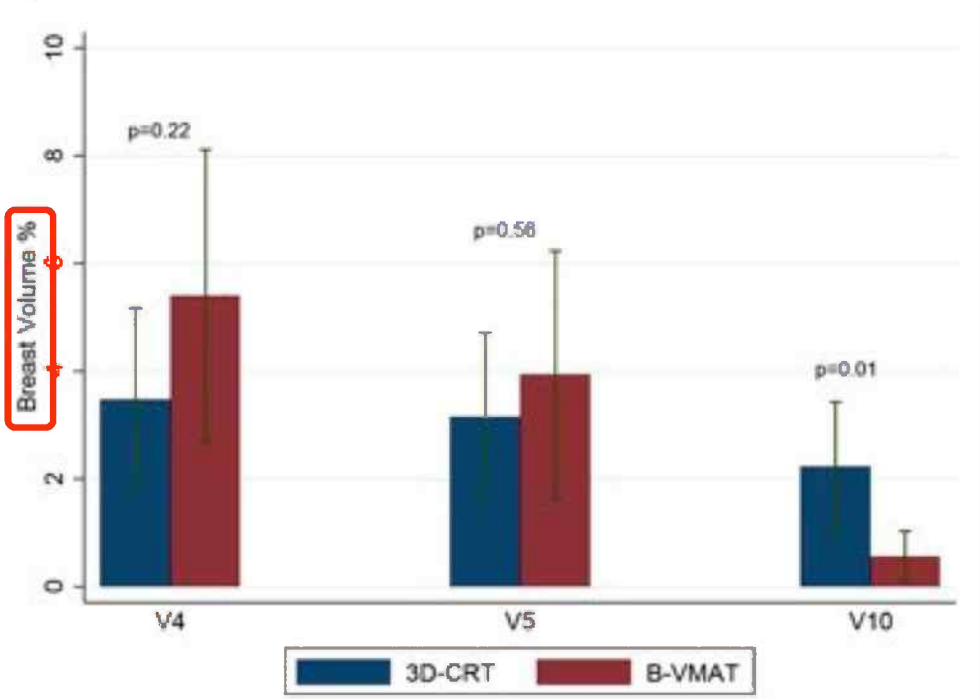
RESULTS

Dosimetric parameters





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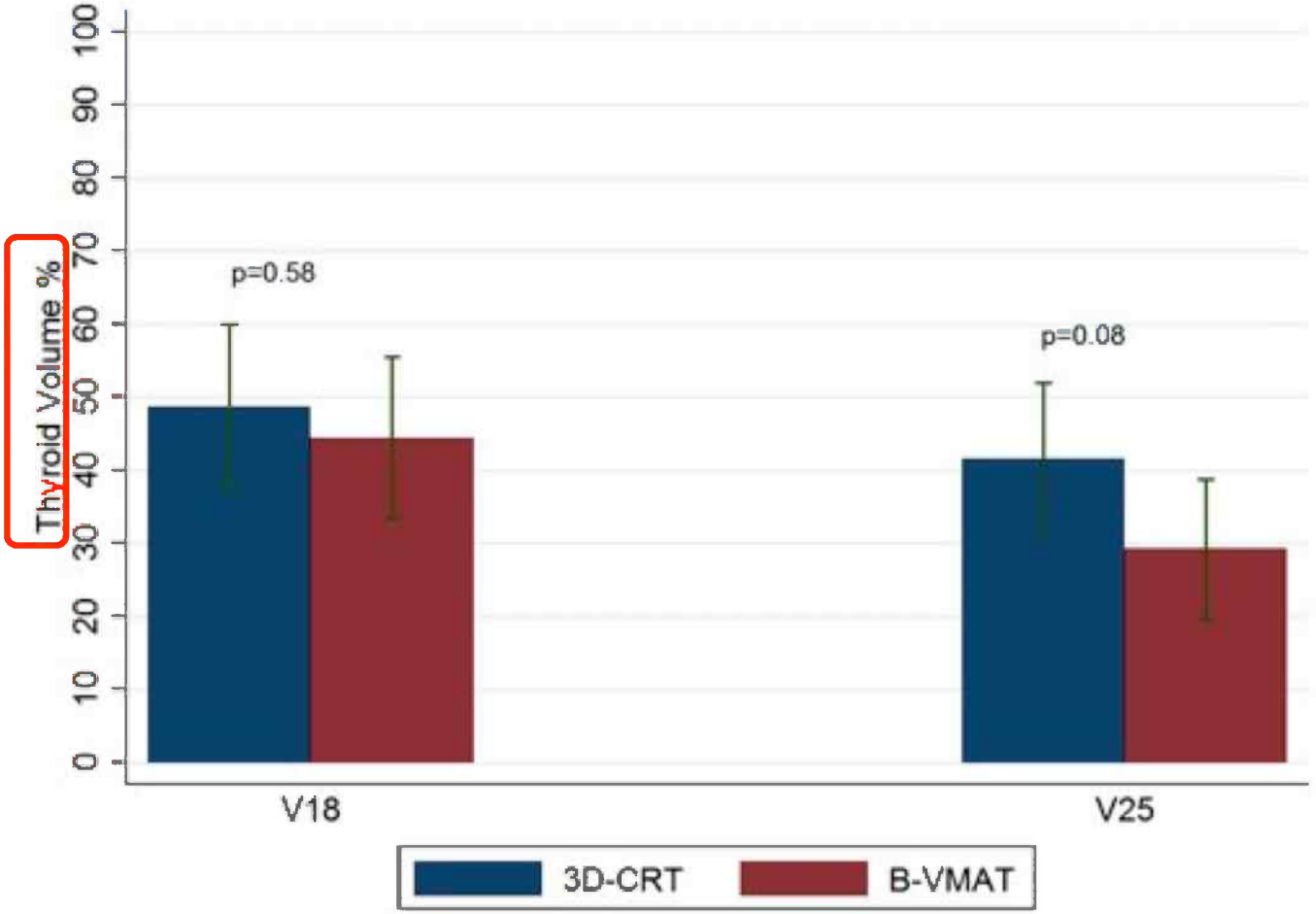
RESULTS

Dosimetric parameters



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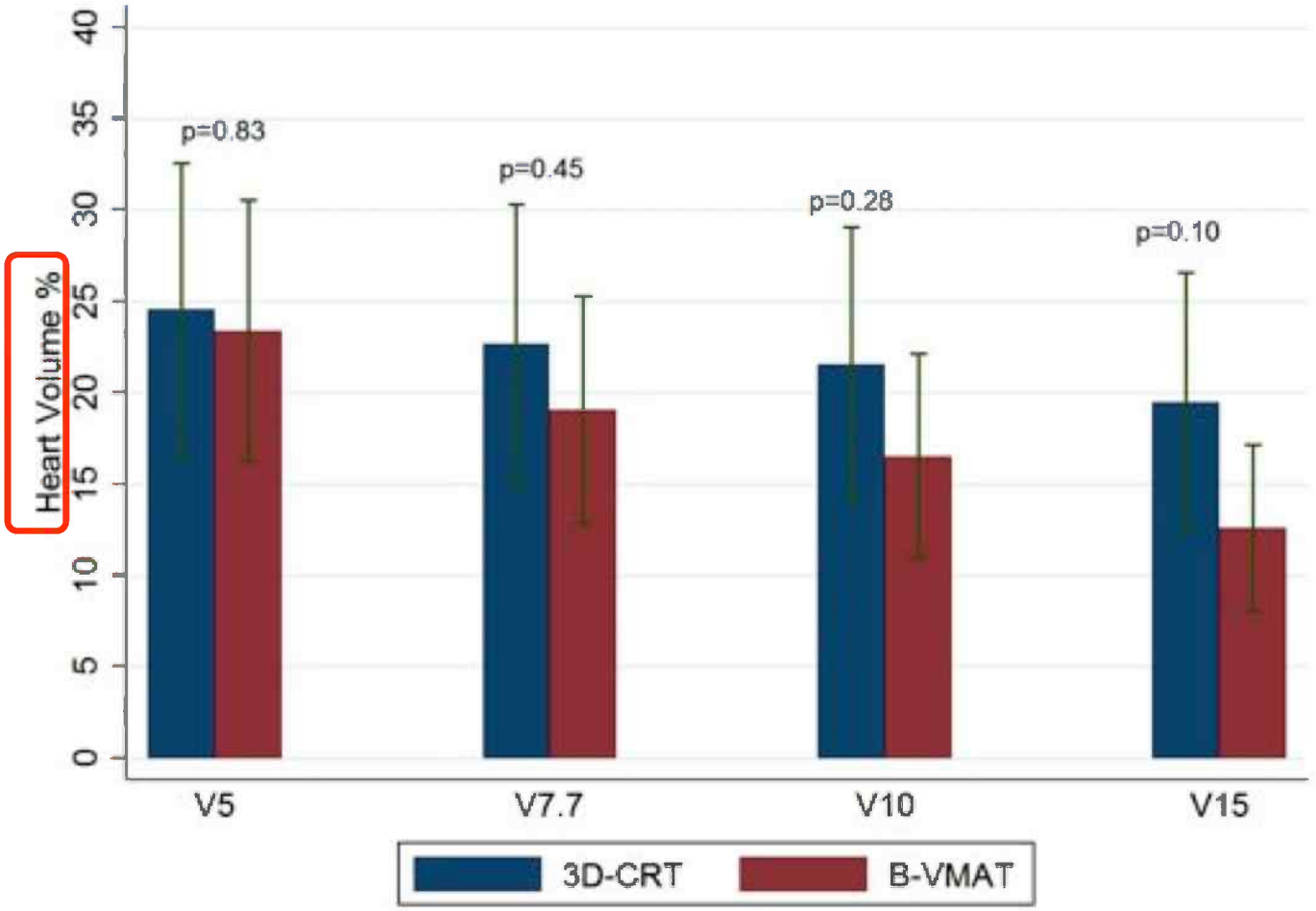
RESULTS

Dosimetric parameters



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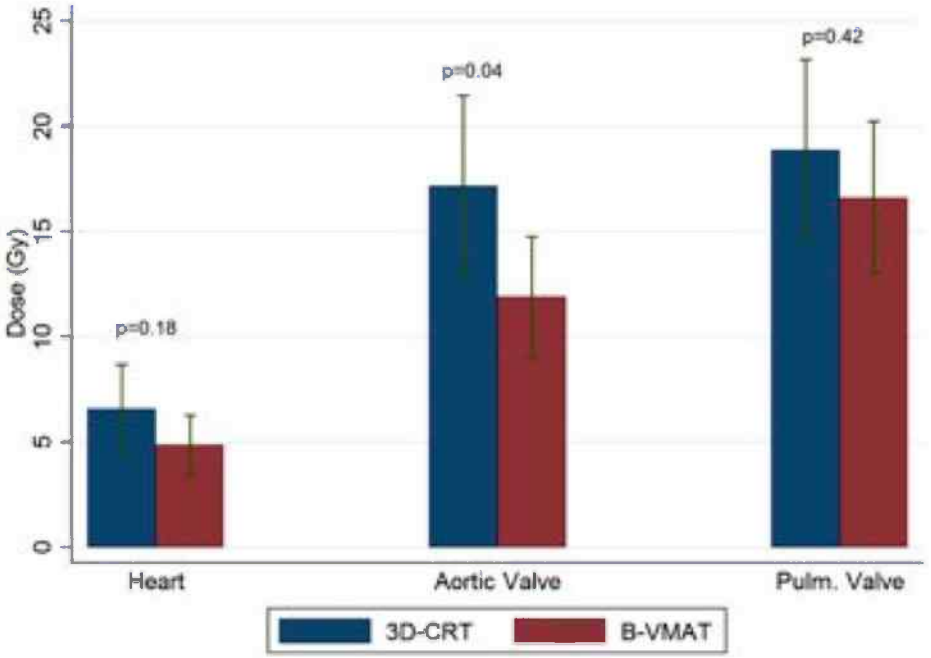
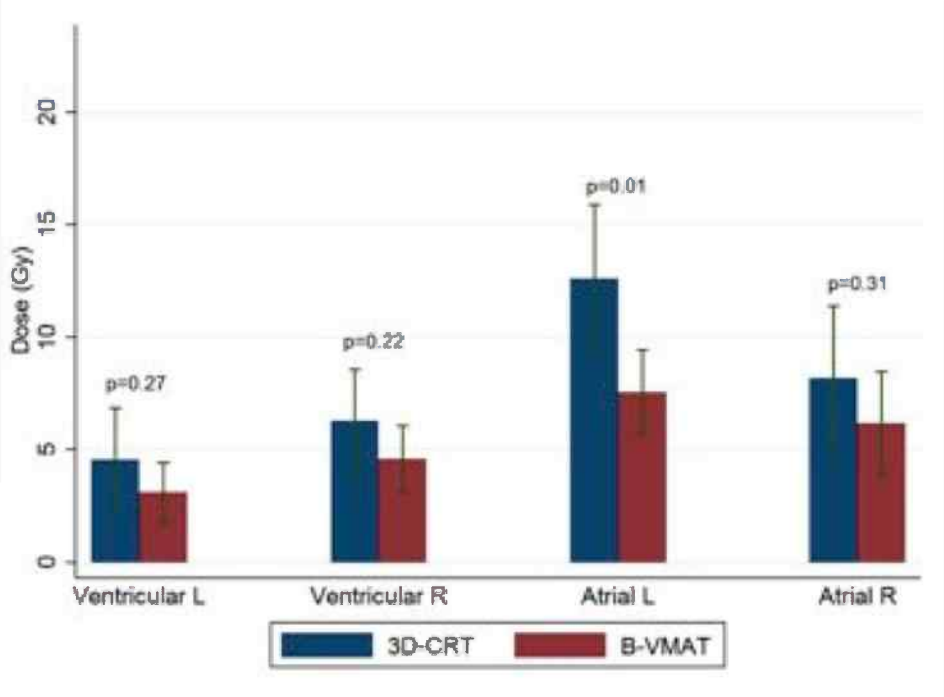
RESULTS

Dosimetric parameters





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RESULTS

Second cancers - OED

	Mean OED and SD		
	3D-CRT	**VMAT**	***p* value**
LUNG			
All	2.16 ± 0.84	2.28 ± 0.73	0.025
No Neck	1.59 ± 0.73	1.91 ± 0.62	0.001
Unilateral Neck	2.31 ± 0.85	2.46 ± 0.81	0.03
Bilateral Neck	2.33 ± 0.76	2.22 ± 0.57	0.23
BREAST			
All	0.22 ± 0.15	0.22 ± 0.16	0.72
No Neck	0.17 ± 0.13	0.20 ± 0.13	0.34
Unilateral Neck	0.26 ± 0.18	0.25 ± 0.19	0.88
Bilateral Neck	0.20 ± 0.12	0.16 ± 0.09	0.02
THYROID			
All	3.29 ± 1.77	3.34 ± 1.75	0.35
No Neck	0.30 ± 0.16	0.41 ± 0.36	0.29
Unilateral Neck	3.65 ± 0.83	3.73 ± 0.81	0.48
Bilateral Neck	4.83 ± 0.62	4.83 ± 0.68	0.94

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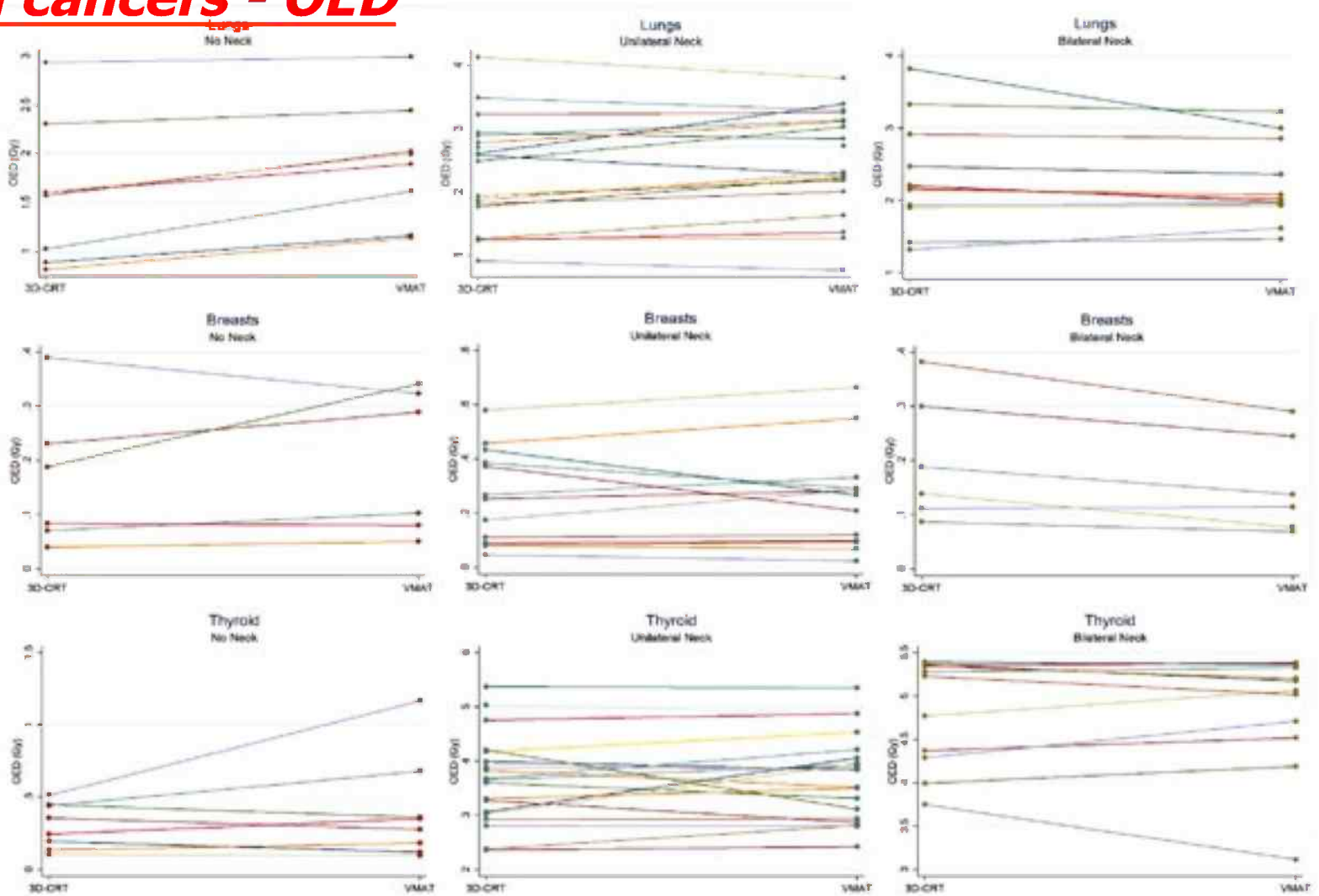
RESULTS

Second cancers - OED



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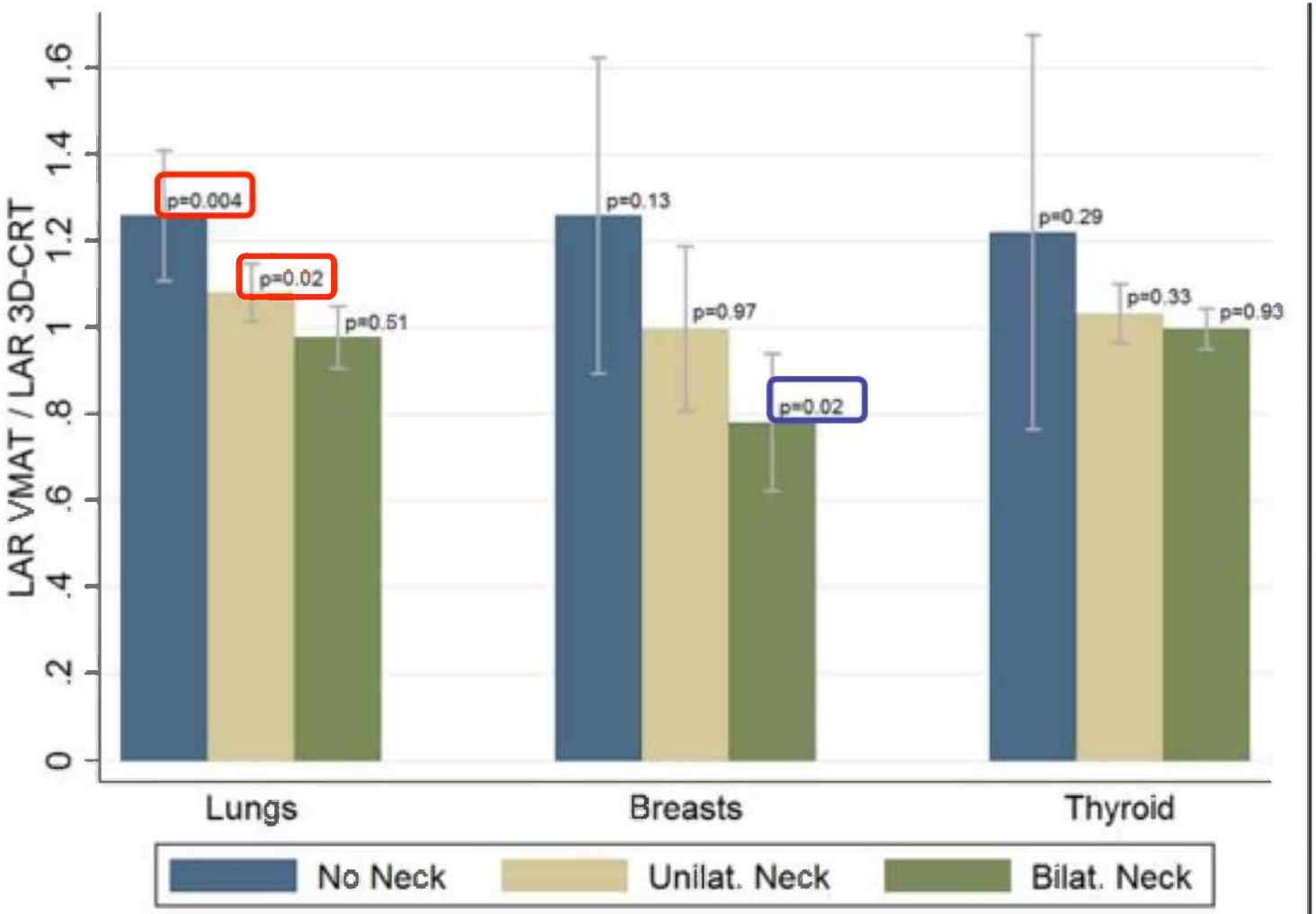
RESULTS

Second cancers - LAR



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RESULTS

Cardiovascular disease - AER

	Mean AER and SD		
	3D-CRT	**VMAT**	***p* value**
Cardiac disease	0.74 ± 1.50	0.37 ± 0.45	0.038
Aortic valve	2.15 ± 2.27	0.26 ± 0.63	<0.0001
Pulmonic valve	3.13 ± 3.24	1.36 ± 1.88	<0.0001
Mitral valve	0.29 ± 1.10	0.003 ± 0.007	0.12
Tricuspid valve	0.73 ± 2.11	0.07 ± 0.36	0.045
All valves	1.57 ± 2.55	0.42 ± 1.14	<0.0001

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CONCLUSIONS

B-VMAT was on average superior to 3D-CRT in terms of lowering the risk of cardiac toxicity

No differences were recorded between 3D-CRT and B-VMAT for thyroid and breast cancer induction, while for lung cancer B-VMAT resulted to be at slightly higher risk

These findings are influenced by the different anatomical presentations, and the data support an individualized approach to early stage HL

The further logical step would be the introduction in the clinical routine of a decisions supporting tool considering all different late toxicity endpoints

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Grazie per l'attenzione...

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