Dipartimento Integrato Interistituzionale
DIPINT

Primo Workshop

Clinical Research and Innovation

Venerdì 4 luglio 2014 9,00 - 19,00

Aula Magna - Polo Fibonacci - Largo Pontecorvo 3, Pisa

Lung cancer screening with low-dose computed tomography (CT): the ITALUNG-CT study and a demonstration project for lung cancer's early diagnosis in Tuscany.

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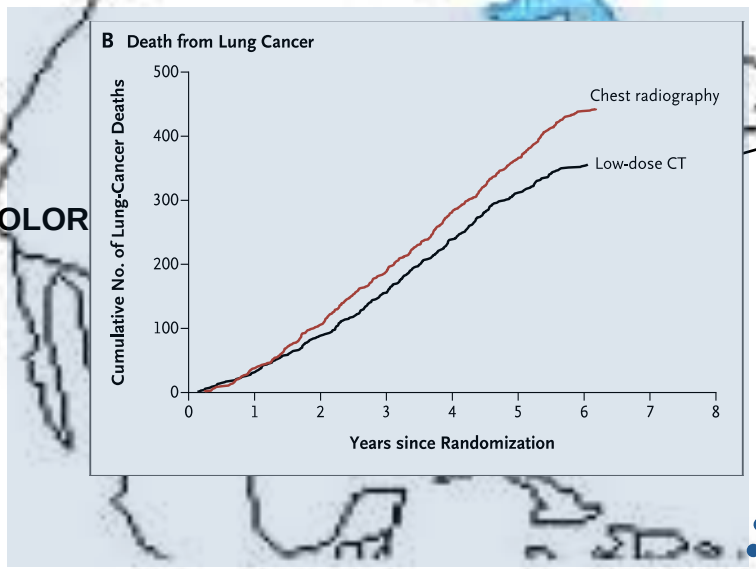
AOUP

LUNG CANCER SCREENING TRIALS



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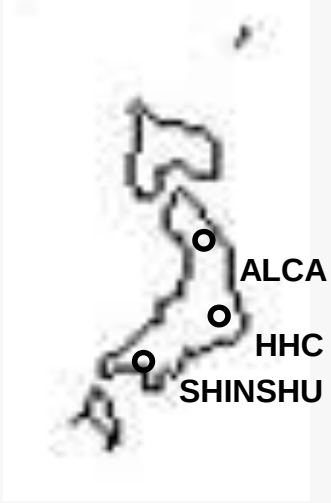
CONCLUSIONS

Screening with the use of low-dose CT reduces mortality from lung cancer.



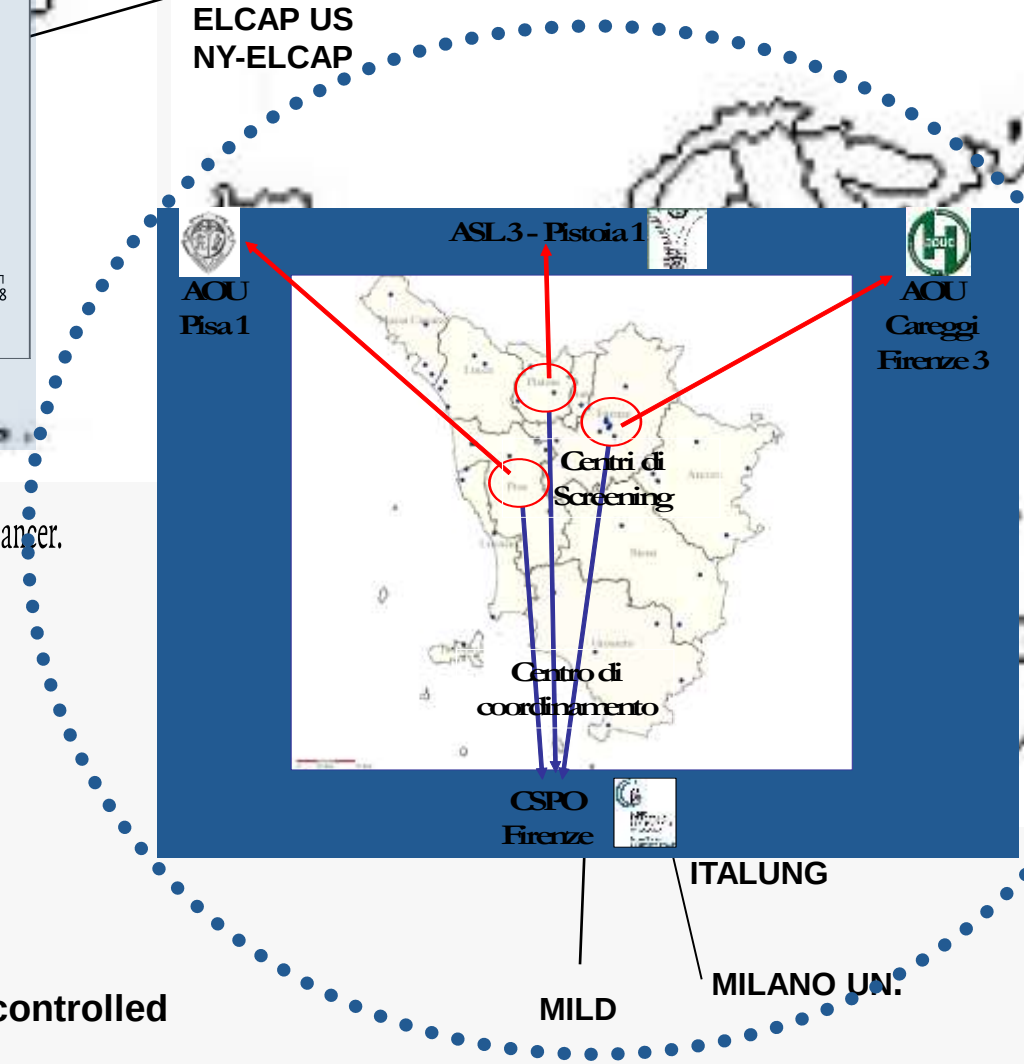
ALCA

HHC

SHINSHU UN.

° One harm

* Randomised controlled



ITALUNG CT Study

PRIMARY OUTCOME

- Lung cancer mortality

STUDY DESIGN

- Multicentre randomised controlled trial with low-dose CT (LDCT) vs usual care.
- Funded by Regional Health Public Authority
- Recruitment: 2004 –2006
- Data collection: 2004- 2009
- LDCT baseline, 1°,2°,3° annual repeat: T0-T1-T2-T3
- Standardised protocol for management of positive CT (nodule's detection)
- Free access to a smoking cessation program
- Follow up 2009-2015 (Tuscany cancer registry, GP, current

Lopes Pegna et al, Lung Cancer 2009

ITALUNG-CT: results

	Baseline T0	1° Repeat T1	2° Repeat T2	3°Repeat T3	Total Repeat T1-T3
N. Subjects	1406	1356	1308	1263	3927
Positive LDCT %	30,3	17	16	14	16
N. screen detected Lung cancer	21	5	7	5	17
SCLC (Small Cell Lung Cancer)	2	1			3
N. Interval lung cancer					2
Detection rate (%)	1.49	0.29	0.49	0.35	1.37
Stage I (%)	55.6	60.0	50.0	80.0	61.1
Adenocarcinoma (%)	47.6	25.0	85.7	100	70.5
Surgery (%)	80.9	80.0	100	80.0	88.2

Lopes Pegna et al, J Thorac Oncol 2013

ITALUNG-CT: Bio-markers analyses

Table 3
K-ras and p53 mutations analysis, plasma DNA (cut-off 5 ng DNA/ml plasma), allelic imbalance in subjects at baseline CT Scan.

Biological specimen	Molecular test	Negative at baseline CT, *N* = 38	Recalled for assessment or follow-up, *N* = 37	Lung cancer, *N* = 19
		N (%)		
Sputum	K-ras mutation	1 (2,6%)	0	3 (15,8%)
	P53 mutation	0	0	2 (10,5%)
	Allelic imbalance positive	10 (26,3%)	27 (73,0%)	16 (84,2%)
Plasma	K-ras mutation	0	1 (2,7%)	8 (42,1%)
	P53 mutation	0	0	0
	Plasma DNA with cut-off ≥5 ng DNA/ml plasma	10 (26,3%)	11 (29,7%)	14 (73,7%)
	Allelic imbalance positive	5 (13,2%)	4 (10,8%)	11 (57,9%)
Sputum and/or plasma	K-ras mutation	1 (2,6%)	1 (2,7%)	10 (52,6%)
	P53 mutation	0	0	2 (10,5%)
	Allelic imbalance positive	11 (28,9%)	27 (73,0%)	17 (89,5%)

Allelic imbalance, free-circulating plasma DNA quantification and K.ras mutation could be jointly useful to identify, between smokers and ex-smokers, the subjects at major risk for lung cancer.

A multi-screening approach integrating imaging technique and a biomolecular marker panel is worth of further investigation. The use of early biomarkers would integrate the assessment of the individual lung cancer risk.

F Carozzi,et al, Lung Cancer 2009

ITALUNG-CT: smoking cessation intervention

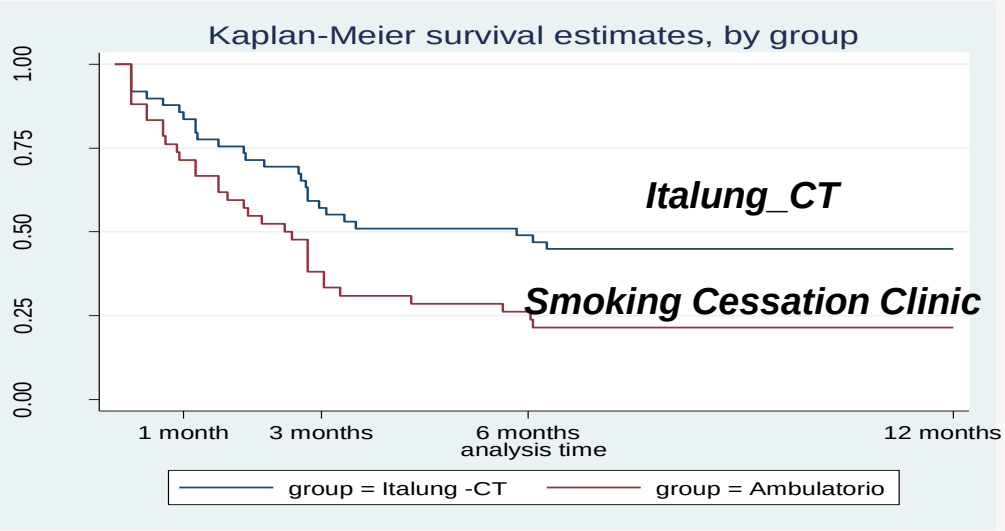
Smoking cessation rates

n	**Active harm**	**Controls**
	170 (1) / 818 (2)	**149 (1) /894 (2)**
%	**20.8**	**16.7**

p = .003

(1) = "quitters" (current smokers at T0 >>> abstinent from smoking at T3)
(2) = current smokers at T0

Smoking cessation is a high priority for patients who are currently smoking. Cessation's interventions must be integral part of the screening studies/programs



Pistelli et al, ERJ 2012

Continuous abstinence in Italung CT subjects and in subjects attended smoking cessation clinic

ITALUNG-CT: assessment of smoking induced emphysema with LDCT

Longitudinal quantitative analysis of the TC detected emphysema during the study: multivariate regession model

VARIABILI INDIPENDENTI	COEFFICIENTE	P	IC 95%
Età	-0.613	0.007	[-1.061 ; -0.165]
ppFEV1	0.108	0.038	[0.005 ; 0.211]
Sesso maschile	-13.032	0.000	[-17.364 ; -8.699]
Ex Fumatori Persistenti	-12.783	0.000	[-16.969 ; -8.597]
Quitters	-6.269	0.023	[-11.667 ; 0.872]
PY mediana	-2.096	0.270	[-5.819 ; 1.627]

- Smoking cessation seems to be related to a reduction in lung density (inflammation?).
- Assessment of the impact of smoking related damage.
- Early identification of smoking related disorders other than cancer

ITALUNG-CT: perspectives

International workshop on lung cancer screening randomised trial.
State of the art in Europe after the early stop of the US NLST trial.
Pisa (Italy), 4th March, 2011

The PISA Position Statement

- The shared opinion of the trial investigators is that **European trials should continue and evaluate the full effect of screening with low-dose CT** scan compared with non-screening (usual care) populations, in terms of **mortality reduction as well as cost/benefit effects**.

- The EUCT investigators consider, while the European trials will continue until the scheduled end, extremely important the launch of **demonstration projects aimed to evaluate essential aspects of the CT Scan lung cancer screening process, multi-centric and coordinated at European level.**

- At individual level, **spontaneous access to CT Scan lung cancer screening should be discouraged at the moment**, considering the available evidence still insufficient to suggest its use outside a controlled, research setting.

ITALUNG-CT: perspectives

Lung cancer screening program in high risk subjects in Tuscany: demonstration project

- Recruitment by GP and at work health service; standardised web-administered questionnaire for eligibility (smoking, work exposure)
- Risk assessment in screening centre: questionnaire, lung function, blood/sputum sample.
- Smoking cessation intervention
- Enrolment in the screening program: LDCT CAD
- Centralised double reading by network of the digital imaging
- Standardised management of positive LDCT: integrated centralised approach (radiologists, pathologists, pulmonary physicians, thoracic surgeons)

Aim is a **Health Technology Assessment project** to produce recommendations for the quality and appropriateness of the possible lung cancer screening.

The basic feature of this **new *e-screening* is the via web integration and sharing of the different professional skills developed within the ITALUNG-CT n 1 study.**

ITALUNG CT STAFF and AFFILIATIONS

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Disclosure: The authors declare no conflict of interest.

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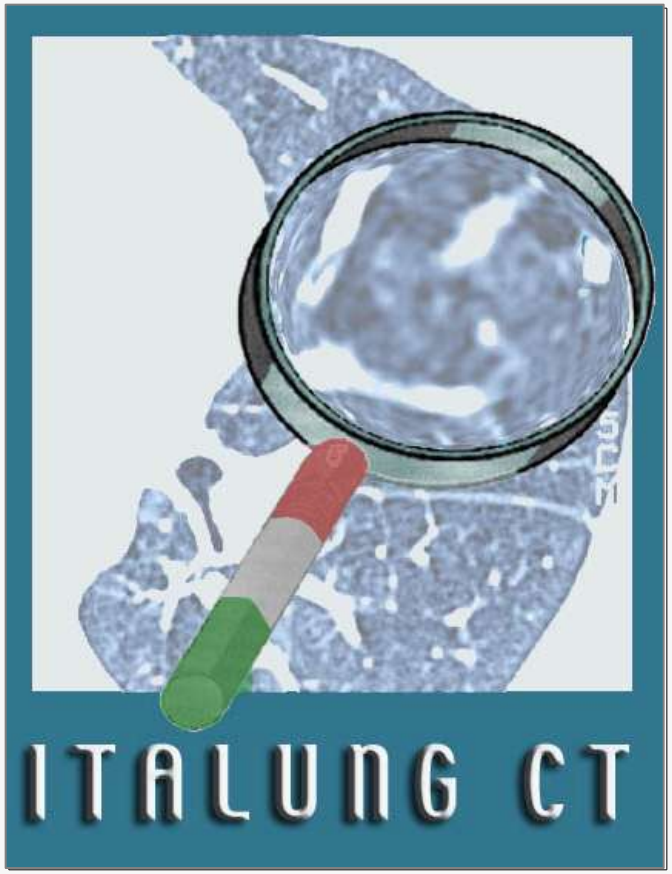

Thank you for your attention!