Potential collaboration in Sino-US EDRN lung cancer biomarker

Objective:

Lung cancer is the leading cause of cancer death both in the USA and China. The survival rate is closely related to the stage at diagnosis, which is more favorable when diagnosed at an earlier stage. The results of the National Lung Cancer Screening Program have demonstrated a 20% reduction in lung cancer mortality using low dose spiral CT (LDCT) among heavy smokers. Based on this result, some medical organizations have revised the guidelines for lung cancer screening. However, there are still some harms of LDCT screening that can not be neglected: 1) false positive results which may lead to unnecessary further diagnostic work-up including biopsy and anxiousness; (2) intensive CT scans may increase cancer risk from radiation. Recent advances have facilitated biomarker discovery for early diagnosis of lung cancer through the analysis of surrogate tissues, including airway epithelium, sputum, exhaled breath, and blood. Although a number of candidate diagnostic biomarkers have been described, none have been validated for use in a clinical setting.

The specific aims of the study are:

1) Establish a multi-center screening cohort based on the LDCT lung cancer screening program in rural China for development and validation of biomarkers to augment CT diagnosis of lung cancer;
2) Prospective validation of the promising biomarkers discovered in previous case-control studies in multi-center lung cancer screening cohort in China;
3) Evaluate the utility of screening markers to augment CT diagnosis of lung cancer;
4) Evaluate the utility of risk markers to predict lung cancer risk combined with personal factors for the optimal selection of high risk populations.

Resources available:

In 2010, a population-based prospective, LDCT lung cancer screening program in rural China was initiated. This program was funded by The Chinese Central Government Public Health Special Subsidy. This program has established a multi-center lung cancer screening cohort which will facilitate biomarker validation in

a prospective design. Figure 1 illustrates the organization and implementation of the program.

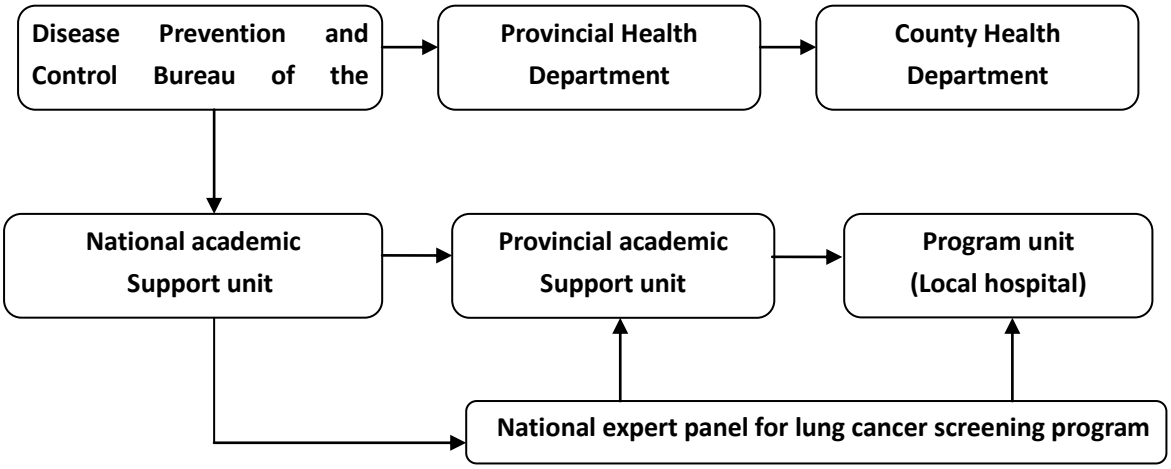

Figure 1 Organization and implementation of lung cancer screening program

Since 2010, the number of screening sites have increased from 2 to 6 districts or counties in 2 provinces(Yunnan, Sichuan) and two Municipalities (Beijing, Tianjin), and will expanded to 9 districts or counties in the year 2015. Table 1 shows the time schedule of LDCT lung cancer screening in rural China.

Table 1 Time schedule of LDCT lung cancer screening in rural China

Time	No of screening site	Screening cite	Scheduled No. of screening
2010.1-2011.16	2	Dagang, Tianjin	1000
		Xuanwei,Yunnan province	1000
2011.7-2012.6	2	Dagang, Tianjin	1000
		Xuanwei,Yunnan province	1000
2012.7-2013.6	3	Dagang, Tianjin	1000
		Xuanwei,Yunnan province	1000
		Beijing	1000
2013.7-2014.6	6	Dagang, Tianjin	2000
		Xuanwei,Yunnan province	2000
		Beijing	1000
		Gejiu, Yunnan province	1000
		Nanchong, Sichuan province	1000
		Chengdu, Sichuan province	1000

In this program, the criteria for high-risk populations are defined according to

smoking history (≥20 pack-years), age distribution, and other risk factors in different regions and centers. By the end of July, 2014,a total of 10440 individuals received baseline screening, and 144 lung cancer cases were detected with a detection rate of 1.38. In 144 lung cancer cases, 52 cases were early lung cancer (36.11%). Primary results of baseline screening are shown in table 2. In Dagang and Xuanwei screening cite, about 60% of the participants receivedannual screening examinations, 32 lung cancer cases were detected with a detection rate of 0.39%(in person-year), and 75% were early lung cancers(table 3).

Table 2 Results of baseline screening in rural China

Province	site	Time	subject	case	Detection rate（%）	No of early lung cancer	Early detection rate（%）	No of treatment	Treatment rate（%）
Tianjin	Dagang	2010	1000	4	0.40	3	75.00	3	75.00
		2010.7-2011.6	1000	9	0.90	4	44.40	8	88.90
		2011.7-2012.6							
		2012.7-2013.6	1082	6	0.57	2	33.30	3	100.00
		2013.7-2014.6	245	0	0	0	0	0	0
		Total	3227	19	0.57	9	47.23	17	89.47
Yunnan	Xuanwei	2010	1000	29	2.9	6	20.69	18	62.07
		2010.7-2011.6	1000	29	2.90	7	24.14	18	62.07
		2011.7-2012.6							
		2012.7-2013.6	2014	57	2.83	24	42.11	40	70.18
		Total	4014	115	2.87	37	32.17	76	66.09
Yunnan	Gejiu	2013.7-2014.6	1018	6	0.59	4	66.77	6	66.77
Sichuan	Nanchong	2013.7-2014.6	1050	2	0.19	2	100	2	100
	Chengdu	2013.7-2014.6	1031	2	0.19	0	0	1	0
Total			10440	144	1.38	52	36.11	99	68.75

Table 3 Results of annual screening in rural China

Province	site	Time	subject	case	Detection rate（%）	No of early lung cancer	Early detection rate（%）	No of treatment	Treatment rate（%）
Tianjin	Dagang	2010							
		2010.7-2011.6							
		2011.7-2012.6	1095	5	0.46	5	100.00	5	100.00
		2012.7-2013.6	1067	3	0.28	3	100.00	3	100.00
		2013.7-2014.6	1785	3	0.17	3	100.00	3	100.00
		Total	3947	11	0.28	11	100.00	11	100.00
Yunnan	Xuanwei	2010							
		2010.7-2011.6							
		2011.7-2012.6	1005	3	0.30	2	66.67	2	66.67
		2012.7-2013.6	0	0	0.00	0			
		2013.7-2014.6	3162	18	0.57	11	61.11	16	88.89
		Total	4167	21	0.50	13	61.90	18	85.71
Total			8114	32	0.39	24	75.00	29	90.63

Although the effectiveness of LDCT screening has been confirmed, questions remain regarding the definition of high-risk populations, high false positive rates, and radiation risk. Molecular markers may be helpful for risk prediction, and in combination with LDCT in lung cancer screening may reduce high false positive results. Based on the LDCT screening in rural China, we are establishing a multi-center screening cohort which will provide great opportunity for prospective validation of biomarkers and investigation of the complement role of biomarker for LDCT in lung cancer screening.

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