

Technical Note

On Spatial Relations for Non-small Cells Lungs Cancer Interpretation

Nadeem Salamat^{1,*}, V. B. Surya Prasath^{2,3,4} and Malik M. Saad Missen⁵

¹ Department of Basic Sciences and Humanities, Khawaja Fareed University of Engineering and Information Technology, Rahim Yar Khan, Pakistan; nadeem.salamat@kfueit.edu.pk

² Computational Imaging and Visualization Analysis Lab, Department of Computer Science, University of Missouri-Columbia, Columbia MO 65211 USA; prasaths@missouri.edu

³ Division of Biomedical Informatics, Cincinnati Children's Hospital Medical Center (CCHMC), Cincinnati, OH 45229 USA

⁴ Department of Biomedical Informatics, College of Medicine, University of Cincinnati, OH USA

⁵ Department of Computer Science and Information Technology, The Islamia University of Bahawalpur, Pakistan; saad.missen@iub.edu.pk

* Correspondence: nadeem.salamat@kfueit.edu.pk; Tel.: +92-332-686-8106

Abstract: Computers and artificial intelligence affect every field of life nowadays. In medical image interpretation automatic decision making using algorithms are used increasingly in every sub-field and computer aided diagnosis (CAD) is one of the main tools available to medical science today. CAD systems are used as an augmented option for both the medical practitioner and the patients, with image analysis and interpretation being of primary importance. In particular, spatial relations are used in knowledge representation, and these relations can be used for effective medical image interpretation. In this paper, we put forth an algorithm for defining non-small cells lungs cancer (NSCLC) stages in lungs images interpretation using topological spatial relations. We show an application case study in event motion predictions for lung cancer staging scoring - tumor, nodes and metastasis (TNM) - with combined topological and directional relations.

Keywords: computer aided diagnosis; topological relations; TNM system; non-small Cells; lung cancer

1. Introduction

Nowadays pulmonary diseases are increasing rapidly due to certain environmental conditions as well as man-made scenarios. One of the major among pulmonary diseases is the lung cancer that is growing rapidly with the passage of time and has drastic impacts and major causes of mortality in world [1]. According to a WHO study, while breast cancer causes the highest rate of death of women in Pakistan and second highest is the lung cancer whereas in men lung cancer is the highest rate of death. Taken as a whole, lungs cancer is the highest cause of deaths in Pakistan for both sexes. Lung cancer is one of the major respiratory system disease, which cause difficulty in breathing. From the advent of the twentieth century, lung cancer is proliferating rapidly. Lung cancer is now the second most common type of cancer worldwide. It is caused by various factors, and the most common cause of happening is due to smoking but an individual has chances of having cancer even if he or she does not indulge in smoking, with symptoms and causes varying accordingly. However, smoking is considered a major reason for lung cancer. The latest studies shows that ratio of smokers and non-smokers individuals having a chances of lungs cancer is 10:1. Cancer can grow in both or in one of the lungs. Cancerous cells can grow and replicate itself into other body parts as well. With the passage of time, tumor cells grow large in cells and create disturbance in lungs activities. There are various kinds of lung cancer.

29 Primary lung cancer starts from lungs whereas a cancer that starts from neighboring body part and
30 spread to the lungs after metastasizes in body is termed as secondary lung cancer. When lungs going
31 through discomfort, their ability to bloodstreams decline.

32 Different imaging techniques are used in clinical applications. The computers are introduced
33 to these applications for automatic image interpretation and diseases diagnosis. Medical images
34 acquisition used for these applications is two dimensional (2D), three (3D) dimensional, or higher
35 dimensions. These techniques are magnetic resonance imaging (MRI), magnetoencephalography
36 (MEG), 3D ultra sound imaging, computed tomography (CT), positron emission tomography (PET),
37 single photon emission computed tomography (SPECT), functional MRI (fMRI), and diffusion weighted
38 imaging (DWI). These detailed amount of information needs most modern techniques of medical
39 image interpretation to provide better diagnosis and treatment options for clinical applications. It
40 requires significant innovation in all aspects of image processing, such as image segmentation, image
41 registration, visualization, compression and communication and interpretation.

42 Computer-aided diagnosis (CAD) provides a computerized diagnostic result and these results
43 are used as a second opinion for the patients. The CAD assist radiologists in the diagnosis of diseases
44 using the image analysis methods. Presently, CAD is used in the area of detection of breast cancer in
45 mammograms, these algorithms are extendable for lungs images also. Currently, a large research effort
46 has been devoted to the detection and classification of various lung diseases in thoracic computed
47 tomography (CT) images. In CAD schemes in thoracic CT, nodule detection, distinction between
48 benign and malignant nodules, and detection, characterization, and differential diagnosis of diffuse
49 lung disease are included. The CAD schemes are used in clinical practice by providing radiologists
50 with computer output as a *second opinion*. These schemes are further extendable for cancer staging and
51 can be used to detect the development of changes in cancer stages. After the detection and labeling
52 stage, the PET /CT images are segmented. Then the cancer staging is defined [2],[3], [4], these stages
53 are performed manually by imaging experts. These stages depend upon the size, shape and location
54 of the Tumor[1]. In this paper, we propose an automatic image interpretation algorithm to define the
55 Lungs cancer stages.

56 The number of methods have been introduced to detect the lungs cancer in images in CT and
57 PET images by method developed in [5,6]. The PET integrated images in the cancer grading (TNS)
58 system are used to detect the tumors[4]. In the TNM lungs cancer staging T is used as the size of the
59 tumor, N is used as the Lymph Node status and M is the abbreviation of distant Metastasis [7]. The
60 eighth edition of the TNM staging system has been officially accepted by the Union for International
61 Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC). Although, the AJCC
62 has delayed its implementation of the eighth edition of the staging system until 2018. In case of Non
63 Small Cell Lung Cancer (NSCLC), the early staging of the diseases is crucial and it helps the Doctor to
64 propose the proper medication and therapy. The medication for lungs cancer is prescribed according
65 to its known type and its stage. Various treatments are available for different kinds of cancer.

66 The spatial relations are actively used in many fields of image analysis and knowledge
67 representation. These class of relations is further studied in the multiple contexts of metric relations and
68 directional relations. Topological relations is subclass of metric relations. The topological relations are
69 developed in [8,9] using the point set topology approach and region connected calculus (algebraic point
70 of view) in [10–12]. These relations vary from region to region pairs [13,14]. [15]. The change in the
71 spatial position of objects is exploited by the topological changes between objects in images[13,16–18]
72 and reasoning about these changes are argued in [19]. The spatial relations are defined in image objects
73 after the segmentation and labeling of objects. During the segmentation and labeling stage, the objects
74 are segmented and labeled. Then spatial relations are defined between the required object pair. These
75 spatial relations can also be used to define the cancer stages, such as, for defining the primary or
76 secondary lungs cancer, Disjoint or the Tangent Proper Part or Non Tangent Proper Part topological
77 relation can be used. Similarly T staging also depend upon the position of a tumor in lungs, and
78 its growth to the neighboring body parts, this is possible intuitively by determining the Externally

79 Connected (EC) of the lung cancer and the neighboring body part such as spinal bone , heart, ribs etc.
 80 Some relations also need to determine the history of the spatial relations, such as *Reach* relation can be
 81 modeled as initially DC and then EC relation, such as modeled in [20]. In this paper, we develop the
 82 Lungs cancer staging in images based on the spatial relations between body parts.

83 This paper is arranged as follows. Some preliminary definitions, and lungs cancer stages are
 84 discussed in Section 2. Section 3 describes the intersection model of topological relations. Finally,
 85 Section 4 provides the conclusions.

86 2. Lungs Cancer Staging of NSCLC

87 2.1. Preliminary Definitions

88 **Regular closed Sets:** A set A is called regular closed if $A = \overline{\text{Int}(A)}$

Diameter of a set: Diameter of a set A is defined as

$$D(A) = \max \{d(a_1, a_2) | a_1, a_2 \in A\} \quad (1)$$

89 **Definition:** Let A and B be pair of subsets of a topological space X . A topological relation between A
 90 and B is described by a triplet of values (A, B, d) , where d is the topological relation.

91 2.2. TNM System

92 The current system for staging lung cancer is based on the Tumor - Node - Metastasis (TNM)
 93 classification This grading system involves the primary tumor (T), the degree of lymphnode
 94 involvement (N) and the presence of metastasis (M)[7]. The TNM classification system has been
 95 used as a standard by American joint committee on cancer to help doctors to identify the stags and
 96 types of cancer during interpretation. Due to advances in cancer categories every year, TNM system is
 97 upgraded regularly. Tumors, nodes and lymph nodes has been assigned a number or letter in TNM
 98 system. These letters are explained as

99 **T:** Refers to the tumor which is in its initial form or called primary tumor.

100 **N:** Term N indicates whether nearby lymph nodes are effected by cancer or not.

101 **M:** Refers to metastasis. It can predict whether distant parts of body has been effected by cancer or
 102 not.

103 Following is the detail of each system.

104 2.3. T-Staging

105 This staging depends upon the size and location of the tumor in NSCLC in human lungs . Satellite
 106 nodules are also checked in this stage of evaluation. The T category gives information about aspects of
 107 the original (primary) tumor, size, how deeply it has grown into the organ it started in, and whether it
 108 has grown into nearby tissues.

109 Numbers after the T (such as T_1, T_2, T_3 , and T_4) might describe the tumor size and or amount of
 110 spread into nearby structures. The higher the T number, the larger the tumor and/or the more it has
 111 grown into nearby tissues.

112 2.4. N Staging

113 Another important screening is the occurrence of nodal, specifically for the ones who are suffering
 114 from mediastinal issues but do not found diseases of extra thoracic. The N category staging is used to
 115 check if cancer has lead to lymphatic nodes or not, this includes

Table 1. T Staging in Lungs Cancer [21]

S.No.	Stage	Interpretation
1	T_X	Tumor can't be measured
2	T_0	Primary tumor has no evidence
3	T_{is}	The cancer cells are only growing in the most superficial layer of tissue, without growing into deeper tissues This may also be called in situ cancer or pre-cancer
4	T_{1a}	Cancer is 1cm or less at its widest part (Diameter of the tumor)
5	T_{1b}	Cancer is between 1cm and 2cm across.
5	T_{1c}	means the cancer is between 2cm and 3cm across.
6	T_{2a}	Cancer has been reached to nearby lymph nodes, tissues or organs and cancer is between 3cm to 4cm
7	T_{2b}	Cancer size is between 4cm to 5 cm
8	T_3	The cancer is between 5cm to 7 cm or there is more than one tumour in the same lobe of the lung Cancerous cells has been reached to other distant parts of body such as ribs, muscles, cartilage, or the diaphragm, the nerve close to the lung (phrenic nerve) and outer covering of the heart (the pericardium)
9	T_4	The cancer is bigger than 7 cm or it is more than one lobe of the lung It is spread into one of the neighbouring parts the muscle under the lungs (the diaphragm) the area between the lungs in the middle of the chest (the mediastinum), the heart, a major blood vessel the wind pipe (trachea), the nerve that controls the voice box, the food pipe (oesophagus), a spinal bone the area where the main airway divides to go to each lung

Table 2. N Staging in Lungs Cancer

S.No.	Stage	Interpretation
1	N_X	Nearby lymph nodes can't be interpreted and evaluated.
2	N_0	No cancer in nearby lymph nodes.
4	N_1	There are cancer cells in lymph nodes within the lung or in lymph nodes in the area where the lungs join the airway (the hilum).
5	N_2	in the centre of the chest (mediastinum) on the same side as the affected lung or just under where the windpipe branches off to each lung
6	N_3	means there is cancer in lymph nodes: on the opposite side of the chest from the affected lung or above the collar bone or at the top of the lung

116 2.5. M Staging

117 The detection and identification of metastases occurred at distance spaces is another important
118 task in lungs cancer staging. The M staging is described as

Table 3. M Staging in Lungs Cancer

S.No.	Stage	Interpretation
1	M_0	Nearby lymph nodes can't be interpreted and evaluated.
2	M_{1a}	means one or more of the following: there is cancer in both lungs there are areas of cancer around the heart or in the lining around the lung there is fluid around the lung or heart that contains cancer cells, this is called a malignant pleural effusion or a pericardial effusion
4	M_{1b}	There is a single area of cancer outside the chest in an organ (such as the liver or brain) or a lymph node..
5	M_{1c}	There is more than one area of cancer in one or several organs

119 2.6. TNM Grading System

120 The TNM classification of Non Small Cell Lungs Cancer is the classification system developed by
121 the Pieter E. all in ([21]). This system is designed to help efficiently distinguish lung carcinomas from
122 other lung lesions, as well as how cancer stages. The combination of the T, N, and M scores is then
123 used to place a given lesion in one of four disease stages (I-IV).

124 As other factors helps in medications, same like is the case with grading. Grading can also be
125 helpful in treatment decision of patients like other factors such as aging, cancer staging. These stages

Table 4. Over all Staging in Lungs Cancer.

S.No.	Stage	TNMCombination	Interpretation
1	Stage ₀		Nearby .
2	Stage _{1A}	$T_{1a}N_1M_0$ $T_{1b}N_1M_0$ $T_{2c}N_1M_0$	The size of cancer is 3cm or smaller
4	Stage _{1B}	$T_{2a}N_0M_0$	<ul style="list-style-type: none"> •Cancer is between 3cm and 4cm. It is growing into structures such as: main bronchus, visceral pleura • Cancer is blocking the airway, as a result the lung collapse partly or completely
5	Stage _{2A}	$T_{2b}N_0M_0$	Cancer size is between 4cm and 5cm, and no cancer cells in any lymph nodes.
6	Stage _{2B}	T_{1a}, N_1, M_0 T_{1b}, N_1, M_0 T_{1c}, N_1, M_0 T_{2a}, N_1, M_0 T_{2b}, N_1, M_0 T_3, N_0, M_0	<ul style="list-style-type: none"> •The tumor size is between 3 cm - 7 cm, and it has spread to local lymph nodes; or • The tumor is greater than 7 cm in size and has not spread to lymph nodes or •Cancer is not in lymph node, but has spread to local areas such as, diaphragm, phrenic nerve , mediastinal pleura and parietal pericardium. or • the cancer is less than 7cm but there are multiple tumours in the same lobe of the lung.
5	Stage _{3A}	T_{1a}, N_2, M_0 T_{1b}, N_2, M_0 T_{1c}, N_2, M_0 T_{2a}, N_2, M_0 T_{2b}, N_2, M_0 T_3, N_1, M_0 T_4, N_0, M_0 T_4, N_1, M_0	<ul style="list-style-type: none"> •Cancer is up to 5cm in size and has spread to the lymph nodes in the centre of the chest on the same side as the tumour or • it is between 5cm and 7cm and multiple tumour in the same lobe of the lung or • Cancer has spread into one or more of the following areas: the chest wall, the phrenic nerve , mediastinal pleura and parietal pericardium, lymph nodes in the lung or close to the lung or • Cancer is larger than 7 cm. It hasn't spread into lymph nodes but has spread into one or more of, diaphragm, mediastinum, the heart , a main blood vessel, trachea, larynx, oesophagus, a spinal bone, the carina or •Cancer in multiple lobes of the same lung and there might also be cancer cells in lymph nodes close to the affected lung.
6	Stage _{3B}	T_{1a}, N_3, M_0 T_{1b}, N_3, M_0 T_{1c}, N_3, M_0 T_{2a}, N_3, M_0 T_{2b}, N_3, M_0 T_3, N_2, M_0 T_4, N_2, M_0	<ul style="list-style-type: none"> •Cancer is less than 5cm and has spread into lymph nodes in one of these places: the opposite side of the chest from the affected lung, the neck, above the collarbone, Or •Cancer size is between 5cm to 7cm and has spread into lymph nodes in the centre of the chest. Or •Cancer of any size, has spread into lymph nodes in the chest centre, and has spread into any of the areas: chest wall, diaphragm, mediastinal pleura and parietal pericardium. Or • Cancer has spread into the lymph nodes in the chest centre. The lung tumour is more than 7cm or it has spread into a major structure in your chest such as: the heart, trachea, oesophagus , a main blood vessel
7	Stage _{3C}	T_3, N_3, M_0 T_4, N_3, M_0	<ul style="list-style-type: none"> •Cancer is between 5cm and 7cm or has spread into one or more of the following: phrenic nerve, parietal pericardium • and it has spread into lymph nodes: in the centre of the chest on the opposite side from the affected lung or at the top of the lung on the same side or opposite side or above the collar bone or there is more than one tumour in a different lobe of the same lung. Or • Cancer is bigger than 7cm or it has spread into one areas: (i) the diaphragm, (ii) mediastinum, (iii) the heart, (iv) a major blood vessel (v), trachea, (vi) the recurrent laryngeal nerve, oesophagus a spinal bone , the area where the windpipe divides (the carina) • It has spread into lymph nodes in chest center on the opposite side from the affected lung or at the top of the lung on the same side or opposite side or above the collar bone
8	Stage ₄	$AnyT, AnyN, M1a$ $AnyT, AnyN, M1b$ $AnyT, AnyN, M1c$	<ul style="list-style-type: none"> • Cancer in both lungs or the cancer is in the pleura or pericardium or there is fluid around the lungs or the heart that contains cancer cells, Or • Cancer has spread outside the chest to a lymph node or liver or bone. Or •The cancer has spread to several areas in one or more organs

126 can be defined as the intersection of mathematical objects. In this system every object is defined as the
 127 closed set. This set is further divided into topological parts, like boundary, interior and exterior. At the
 128 next step, the topological relations are computed between the every object pair.

129 3. Topological relations for lung cancer staging and proposed method

130 The spatial relations between objects in images are used in many image analysis applications and
 131 medical image interpretation is one of them. [22]. In point set topological notation, these relations
 132 are defined as the intersection of two object as 9 intersections model [17]. In this model, topological
 133 primitives participate in defining the relations between parts, these parts are, closure, boundary,
 134 interior and exterior. For example, an object A can be written into its body parts as A^c (exterior), ∂A
 135 (boundary), and A^0 interior of object A . Relation between two objects is developed by the void \emptyset and
 136 non void intersection $\neg\emptyset$ entries of the matrix.

137 The matrix method represents the set of 9-intersections and each combination of 9 intersections
 138 describes a different topological relation, the 9- intersection can be employed to analyze whether or
 139 not two different configurations have the same topological relation [13,16–18]. Examples of topological
 140 invariants applicable to the 9-intersection are the content (i.e., Region of two body parts is empty or

141 non empty) of a set, the dimension, the number of separations, and the sequence of disconnected
 142 intersections of different dimensions along the boundary. For the 9-intersection mode, the of the
 143 nine intersections was identified as a simple and most general topological invariant. It characterizes
 144 each of the nine intersections by a value (\emptyset) or ($\neg\emptyset$). For example, the 9-intersections based on
 145 empty/non-empty intersections for each configuration is

Disjoint(DC): In this situation, two objects are disjoint and topological parts of both the objects don't intersect each other. In matrix notation, this situation can be described as

$$DC(A, B) = \begin{array}{|c|c|c|c|} \hline \cap & B^c & \partial B & B^o \\ \hline A^c & \neg\emptyset & \neg\emptyset & \neg\emptyset \\ \hline \partial A & \neg\emptyset & \emptyset & \emptyset \\ \hline A^o & \neg\emptyset & \emptyset & \emptyset \\ \hline \end{array} \quad (2)$$

146 **Externally Connected (EC):** Where boundaries intersect but the interiors do not intersect

$$EC(A, B) = \begin{array}{|c|c|c|c|} \hline \cap & B^c & \partial B & B^o \\ \hline A^c & \neg\emptyset & \neg\emptyset & \neg\emptyset \\ \hline \partial A & \neg\emptyset & \neg\emptyset & \emptyset \\ \hline A^o & \neg\emptyset & \emptyset & \emptyset \\ \hline \end{array} \quad (3)$$

Partially Overlap (PO): In this case, the boundaries of both the objects intersect each other, similarly, interiors and exteriors of both objects intersect each other.

$$PO(A, B) = \begin{array}{|c|c|c|c|} \hline \cap & B^c & \partial B & B^o \\ \hline A^c & \neg\emptyset & \neg\emptyset & \neg\emptyset \\ \hline \partial A & \neg\emptyset & \neg\emptyset & \neg\emptyset \\ \hline A^o & \neg\emptyset & \neg\emptyset & \neg\emptyset \\ \hline \end{array} \quad (4)$$

147 **Tangent Proper Part (TPP):** In this situation, the reference region lies inside the targeted region and it
 148 touches the targeted boundary internally and 9 intersections are discussed as

$$TPP(A, B) = \begin{array}{|c|c|c|c|} \hline \cap & B^c & \partial B & B^o \\ \hline A^c & \neg\emptyset & \neg\emptyset & \neg\emptyset \\ \hline \partial A & \emptyset & \neg\emptyset & \neg\emptyset \\ \hline A^o & \emptyset & \emptyset & \neg\emptyset \\ \hline \end{array} \quad (5)$$

Non Tangent Proper Part part Inverse (NTPP): In this situation, the 9 intersection matrix is represented as

$$NTPP(A, B) = \begin{array}{|c|c|c|c|} \hline \cap & B^c & \partial B & B^o \\ \hline A^c & \neg\emptyset & \neg\emptyset & \neg\emptyset \\ \hline \partial A & \emptyset & \emptyset & \neg\emptyset \\ \hline A^o & \emptyset & \emptyset & \neg\emptyset \\ \hline \end{array} \quad (6)$$

Tangent Proper Part Inverse (TPPI): In this situation, boundary of the targeted object touches the boundary of reference object internally and 9-intersection is represented as bellow.

$$TPPI(A, B) = \begin{array}{|c|c|c|c|} \hline \cap & B^c & \partial B & B^o \\ \hline A^c & \neg\emptyset & \emptyset & \emptyset \\ \hline \partial A & \neg\emptyset & \neg\emptyset & \emptyset \\ \hline A^o & \neg\emptyset & \neg\emptyset & \neg\emptyset \\ \hline \end{array} \quad (7)$$

149 **NTPP I:** In this situation, the reference object is smaller in size. It occupies space inside the argument
 150 object. The empty and non empty combination of nine intersections for the Non Tangent Proper
 151 Part Inverse (NTPPI) topological relation is described as

$$NTTPI(A, B) = \begin{array}{|c|c|c|c|} \hline \cap & B^c & \partial B & B^o \\ \hline A^c & \neg\emptyset & \emptyset & \emptyset \\ \hline \partial A & \neg\emptyset & \emptyset & \emptyset \\ \hline A^o & \neg\emptyset & \neg\emptyset & \neg\emptyset \\ \hline \end{array} \quad (8)$$

152 **Equal:** The two objects are equal in size, then the topological relation between two objects is
 153 represented by the point set topology

$x = y$ for every point of the set and its matrix representation will be

$$EQ(A, B) = \begin{array}{|c|c|c|c|} \hline \cap & B^c & \partial B & B^o \\ \hline A^c & \neg\emptyset & \emptyset & \emptyset \\ \hline \partial A & \emptyset & \neg\emptyset & \emptyset \\ \hline A^o & \emptyset & \emptyset & \neg\emptyset \\ \hline \end{array} \quad (9)$$

154 3.1. Segmentation and Labeling

155 The spatial relations are defined between the segmented objects(body part) whose boundaries are
 156 well defined. These objects are considered as the regular sets where the boundary is the part of the
 157 object. The object recognition, segmentation and labeling of objects in an image is a separate problem.

158 During the object recognition stage, segmentation process of the lungs image, the body parts
 159 within the lungs or the close to lungs are segmented and then labeled as bellow and the tumor
 160 itself is labeled as object A . If there are multiple cancers regions are detected then they are labeled
 161 as $A_i, i = 1, 2, \dots, n$. Formally, for a given image, containing objects of interest and a set of labels
 162 corresponding to a set of models known to the system is considered as below

The topological relations used in the ontological of medical images can be renamed as *Inside*, this relation is developed by combining the *TPP* and *NTPP* defined in Eq (5 and Eq(6). If the out put of these relations is stored as 1 and zero , then *Inside* is defined as

$$Inside(A, B) = \max \{TPP(A, B), NTPP(A, B)\} \quad (10)$$

163 Similarly the second relation is defined topologically in Eq(3) .

164 The NSLC staging can be developed using the Spatial relations between the cancerous cells of the
 165 body and different body parts. Once these body parts are segmented and labeled as described in above
 166 scheme, the spatial relations can describe the image contents and the cancer stage. The *reach* relation is
 167 defined in videos. In this case, each time analysis is considered as a snapshot, then if the topological
 168 relation between two consecutive test times is changed from disjoint to the externally connected. The
 169 concatenation of these two spatial relations is marked as the *reach* relation.

170 3.2. Primary and Secondary Cancer Detection

171 Once the objects are detected and labeled, the spatial relation disjoint as described in Eq(2) is
 172 computed between the objects A and the lungs. If this relation holds, then the cancer type is the
 173 secondary. IF the output of this relation is zero, or the partially overlap relationship holds between the
 174 Lungs (O_{19}) and the cancerous object A . In such a case, the cancer type will be based on the origin
 175 place of the cancer object.

176 Similarly a cancer is termed as the primary cancer if computed by the equations (Eq(5) and
 177 Eq(6) holds. Once, it is decided that the cancer is primary, then its stages are determined through the
 178 following process.

Table 5. Objects Labeling at the segmentation stage

S.No.	Label	Body Part
1	O_{1Lu}	upper lobe Left Lungs
2	O_{1Ll}	lower lobe of Left Lungs
2	O_{1Ru}	upper lobe of Right Lungs
2	O_{1Rm}	Middle lobe of Right Lungs
2	O_{1Rl}	Lower lobe of Right Lungs
3	O_{2L}	Left Lungs airway (Main Bronchus)
4	O_{2R}	Right Lungs airway (Main Bronchus)
5	O_{3L}	Membrane covering the Left lungs (Visceral Pleura)
6	O_{3R}	Membrane covering the Right lungs (Visceral Pleura)
7	O_4	Lymph nodes
8	O_5	Chest wall (Diaphragm)
9	O_6	Phrenic nerve
10	O_7	Heart
11	O_8	Outer covering of the heart (Pericardium)
12	O_9	Muscle under the Lungs
13	O_{10}	Central area of chest (mediastinum)
14	O_{11}	Main blood vessel
15	O_{12}	Wind pipe(Trachea)
16	O_{13}	Voice box (Larynx)
17	O_{14}	Food pipe (Oesophagus)
18	O_{15}	Spinal bone (carina)
19	O_{16}	Neck (above the collarbone)
20	O_{17}	Liver
21	O_{18}	Ribs
22	O_{19}	Cartilage
24	O_{20}	the area where the windpipe divides (the carina)

179 3.3. T stages

180 Once the cancer is decided as the primary cancer in lungs then at next stage, the *TNM* cancer
 181 stages are interpreted in terms of spatial relations and size of the tumor. The size of the tumor is
 182 measured as the object recognition stage of the system ends up.

183 The *T* staging in cancer is based on two criteria, which are

- 184 • Size of tumor, this is determined by the equation (1)
- 185 • The intersection of the cancer and the different parts of the lungs.

186 The higher order *T* staging is defined as the intersection of the cancer and the neighboring body parts
 187 of the Lungs. In this table the \vee is used to represent the or (union) and the \wedge represents the and
 188 (intersection) operator. In detail, these are defined as

189 3.4. N Stages

190 In the *N* staging, the spatial relation *partially overlap* between the cancer image in the lungs and the
 191 body parts is defined as Eq.(4). For the N_x and N_0 stages there is empty intersection of the cancerous
 192 part and the lymph nodes

193 3.5. M stages

194 Grading schemas also depends upon cancer type, some cancer types doesn't show compatibility
 195 with such grading system, in this case following terminology is used.

Table 6. T Staging in Lungs Cancer in Terms of spatial relations Between Body Parts

S.No.	Stage	Interpretation
1	T_X	Tumor can't be measured
2	T_0	Primary tumor has no evidence
3	T_{is}	The cancer cells are only growing in the most superficial layer of tissue, without growing into deeper tissues This may also be called in situ cancer or pre-cancer
4	T_{1a}	$D < 1$
5	T_{1b}	$1cm < D < 2cm$
5	T_{1c}	$2cm < D < 3cm$
6	T_{2a}	$[EC(A, O_{2R}) \vee EC(A, O_{2L}) \vee EC(A, O_{3R}) \vee EC(A, O_{3L}) \vee EC(A, O_4)]$ and $3cm < D < 4cm$
7	T_{2b}	$4cm < D < 5cm$
8	T_3	$5cm < D < 7cm$ or $[Inside(A_1, O_{1Lu}), Inside(A_2, O_{1Lu}), \dots] \vee [Inside(A_1, O_{1Li}), Inside(A_2, O_{1Li}), \dots] \vee [Inside(A_1, O_{1Ru}), Inside(A_2, O_{1Ru}), \dots] \vee [Inside(A_1, O_{1Rm}), Inside(A_2, O_{1Rm}), \dots] \vee [Inside(A_1, O_{1Rl}), Inside(A_2, O_{1Rl}), \dots]$ Or, $EC(A, O_5) \vee EC(A, O_6) \vee EC(A, O_8) \vee EC(A, O_9) \vee EC(A, O_{18}) \vee EC(A, O_{19})$
9	T_4	$D > 7cm$ Or $[PO(A, O_{1Lu} \wedge O_{1Li})] \vee [PO(A, O_{1Ru} \wedge O_{1Rm})] [PO(A, O_{1Rm} \wedge O_{1Rl})]$ Or $PO(A, O_5) \vee PO(A, O_7) \vee PO(A, O_{10}) \vee PO(A, O_{11}) \vee PO(A, O_{12}), PO(A, O_{13}) \vee PO(A, O_{14}) \vee PO(A, O_{15}) \vee PO(A, O_{20})$

Table 7. N Staging in Lungs Cancer in Terms of spatial relations Between Body Parts

S.No.	Stage	Interpretation
1	N_X	Nearby lymph nodes can't be interpreted and evaluated.
2	N_0	No cancer in nearby lymph nodes.
4	N_1	$PO(A, O_4)$
5	N_2	$PO(A, O_{10}) \vee PO(A, O_{2L}) \vee PO(A, O_{2R})$
6	N_3	$PO(A, O_4) \vee PO(A, O_{16}) \vee PO(A, O_{12})$

196 3.6. TNM staging

197 These stages are defined as a combination of T , N and M stages. The T stages defined in table (6)
198 and N stages are defined in table (7) and M stages are defined in table (8). The TNM stages with the
199 spatial relations are combined as described in table 4.

200 3.7. Examples

201 These spatial relations can be used to determine the cancer stage as the following example shows.
202 After the detection stage, the size is measured by the governing equation (1) and suppose $D = 1.5$.
203 This provides an information that tumor size is $3 \leq D \leq 5$. The intersection of the object A_i is taken
204 with the lungs parts. Suppose the $Inide(A, O_{1Lu}) \neq 0$, this shows that the cancer is primary type and
205 its location is in the upper lobe. Its T stages is determined as T_{1b} . If no cancer part is detected in the
206 nearby lymph nodes, i.e. $PO(A, O_i) \neq 0$ $i = 4, 10, 12, 16, 2l, 2R$. This will result as the N stage is N_1 .
207 If the M stage is also M_0 , then the overall stage is $T_{1b}N_1M_0$ which is *Stage – IA*. Further, the spatial
208 relations can also be used to determine the growth or control over the cancer by comparing the current
209 state of the cancer with the previous history of the patient. As in previous part of the example, the
210 states may change to T_{2a} , or T_{2b} depending on growth size. The N stage can change from N_1 to N_2
211 depending on the growth of tumor and it may reduce size depending on the control of the tumor. M
212 stage can be changed from M_0 to M_1 . In this way new stage could be *Stage – IA*, *Stage – IB* or stage
213 *Stage – IIA*.

214 4. Conclusions

215 Spatial relations are increasingly used in many fields of knowledge representation and image
216 interpretation. These relations are also used for interpretation of medical images. The paper is
217 concerned with the application of topological spatial relations for defining the TNM staging the
218 NSCLC. In this paper, an applicable model is proposed for the lungs image interpretation. This can be

Table 8. M Staging in Lungs Cancer in Terms of spatial relations Between Body Parts

S.No.	Stage	Interpretation
1	M ₀	Nearby lymph nodes can't be interpreted and evaluated.
2	M _{1a}	$Inside(A_1, O_{1L}) \wedge Inside(A_2, O_{1R})$ or $Inside(A_2, O_{1L}) \wedge Inside(A_1, O_{1R})$ $PO(A, O_8), PO(A, O_{3R}), PO(A, O_{3L})$
4	M _{1b}	$PO(A, O_{17})$ or $PO(A, O_4)$
5	M _{1c}	There are more that one cancers in multiple body parts

219 used as the second opinion of practitioners in the medical field. This approach will be extended to the
220 interpretation of other types of cancer in images.

221 **Author Contributions:** N.S and V.B.S.P. conceived and designed the spatial relations model for lung cancer
222 staging; N.S, V.B.S.P. and M.M.S.M. discussed the model and wrote the paper.

223 **Conflicts of Interest:** The authors declare no conflict of interest.

224

- 225 1. Hochhegger, B.; Alves, G.R.T.; Irion, K.L.; Fritscher, C.C.; Fritscher, L.G.; Concatto, N.H.; Marchiori, E.
226 PET/CT imaging in lung cancer: indications and findings. *Jornal brasileiro de pneumologia : publicacao*
227 *oficial da Sociedade Brasileira de Pneumologia e Tisiologia*, 2015.
- 228 2. Rankin, S. PET/CT for staging and monitoring non small cell lung cancer. *Cancer imaging : the official*
229 *publication of the International Cancer Imaging Society* **2008**, 8 Spec No A, 27–31.
- 230 3. De Wever, W.; Ceyskens, S.; Mortelmans, L.; Stroobants, S.; Marchal, G.; Bogaert, J. and Verschakelen, J.A.
231 Additional value of PET-CT in the staging of lung cancer: comparison with CT alone, PET alone and visual
232 correlation of PET and CT. *European Radiology* **2007**, 17, 23–32.
- 233 4. El-Hariri, M.A.; Gouhar, G.K.; Refat, A.M. Integrated PET/CT in the preoperative staging of lung cancer: A
234 prospective comparison of CT, {PET} and integrated PET/CT. *The Egyptian Journal of Radiology and Nuclear*
235 *Medicine* **2012**, 43, 613 – 621.
- 236 5. Valente, I.R.S.; Cortez, P.C.; Neto, E.C.; Soares, J.M.; de Albuquerque, V.H.C.; Tavares, J.M.R. Automatic 3D
237 pulmonary nodule detection in {CT} images: A survey. *Computer Methods and Programs in Biomedicine* **2016**,
238 124, 91 – 107.
- 239 6. Kecheril, S.S.; Venkataraman, D.; Suganthi, J.; Sujathan, K. Automated lung cancer detection by the analysis
240 of glandular cells in sputum cytology images using scale space features. *Signal, Image and Video Processing*
241 **2015**, 9, 851–863.
- 242 7. Giron, J.; Lacout, A.; Marcy, P.Y. Dealing with Lung Cancer {TNM} Classification. *Journal of Thoracic*
243 *Oncology* **2016**, 11, e77 – e78.
- 244 8. Egenhofer, M.J. A Formal Definition of Binary Topological Relationships. FODO, 1989, pp. 457–472.
- 245 9. Egenhofer, M.J.; Franzosa, R.D. Point Set Topological Relations. *International Journal of Geographical*
246 *Information Systems* **1991**, 5(2), 161–174.
- 247 10. Clementini, E.; Felice, P.D. Approximate Topological Relations. *International Journal of Approximate*
248 *Reasoning* **1997**, 16, 173 – 204.
- 249 11. Cohn, A.G.; Bennett, B.; G, A.; Gooday, J.; Nicholas.; Gotts, N.M. Qualitative Spatial Representation and
250 Reasoning with the Region Connection Calculus. Proceedings of the DIMACS International Workshop on
251 Graph Drawing, 1994. Lecture Notes in Computer Science, 1997, pp. 89–4.
- 252 12. Salamat, N.; Zahzah, E. 2D Fuzzy Spatial Relations: New Way of Computing and Representation. *Advances*
253 *in Fuzzy Systems* **2012**, 2012, Article ID 167939, 15 pages.
- 254 13. Egenhofer, M.J.; Herring, J.R. Categorizing Binary Topological Relations Between Regions, Lines and
255 Points in Geographic Databases. Departement of Survey Engineering, University of Maine. Technical
256 report, University of Maine, 1994.
- 257 14. Billen, R.; Kurata, Y. Refining Topological Relations Between Regions Considering Their Shapes.
258 Proceedings of the 5th International Conference on Geographic Information Science; Springer-Verlag:
259 Berlin, Heidelberg, 2008; GIScience '08, pp. 20–37.

- 260 15. Zlatanova, S. On 3D Topological Relationships. Int. Workshop on Database and Expert System
261 Applications. IEEE Computer Society Press, 2000, pp. 913–919.
- 262 16. Delafontaine, M.; de Weghe, N.V.; Bogaert, P.; Maeyer, P.D. Qualitative Relations Between Moving Objects
263 in a Network Changing Its Topological Relations. *Inf. Sci.* **2008**, *178*, 1997–2006.
- 264 17. Egenhofer, M.; Mark, D. Modeling Conceptual Neighborhoods of Topological Line-Region Relations.
265 *International Journal of Geographical Information Systems* **1995**, *9*, 555–565.
- 266 18. Egenhofer, M.J.; Al-Taha, K.K. Reasoning about Gradual Changes of Topological Relationships.
267 Proceedings of the International Conference On GIS - From Space to Territory; Springer-Verlag: London,
268 UK, 1992; pp. 196–219.
- 269 19. Cohn, A.G.; Hazarika, S.M. Qualitative Spatial Representation and Reasoning: An Overview. *Fundamenta*
270 *Informaticae* **2001**, *46*, 1–29.
- 271 20. Salamat, N.; Zahzah, E. Combined Topological and Directional Relations Based Motion Event Predictions.
272 Pattern Recognition and Machine Intelligence - 4th International Conference, PReMI 2011, Moscow, Russia,
273 June 27 - July 1, 2011. Proceedings, 2011, pp. 180–185.
- 274 21. Goldstraw, P.; Crowley, J.; Chansky, K.; Giroux, D.J.; Groome, P.A.; Rami-Porta, R.; Postmus, P.E.; Rusch, V.;
275 Sobin, L. The IASLC Lung Cancer Staging Project: Proposals for the Revision of the TNM Stage Groupings
276 in the Forthcoming (Seventh) Edition of the TNM Classification of Malignant Tumours. *Journal of Thoracic*
277 *Oncology* **2007**, pp. 706–714.
- 278 22. Hudelot, C.; Atif, J.; Bloch, I. Fuzzy Spatial Relation Ontology for Image Interpretation. *Fuzzy Sets Syst.*
279 **2008**, *159*, 1929–1951.