XXIII CONGRESSO
AIRO2013

AIRO

‘ONTOLOGIA’ E TUMORE DEL RETTO:

L’uso della tecnologia nella creazione di schemi terapeutici e programmi di follow-up personalizzati

UNIVERSITAS CATHOLICA SACRI CORDIS MEDIOLANI

MAASTRO

Sviluppo tecnologico

Avanzamento diagnostico ⟷ Avanzamento terapeutico

- target terapy cancer specific
- nuovi farmaci
- ↑ aggressivita' dei trattamenti

➢ miglior outcome
➢ ↑ tossicita'
➢ selettivita' dei trattamenti

“One size fits all”

Medicina personalizzata

Concetto di *Ricerca*

OGGI:

Linee guida e protocolli

Studi clinici randomizzati

Definizione ab initio delle variabili da analizzare

Evidenze ottenute solo per un sottogruppo di pazienti

DOMANI:

Raccolta di variabili correlate con la patologia

Ontologia

Large database

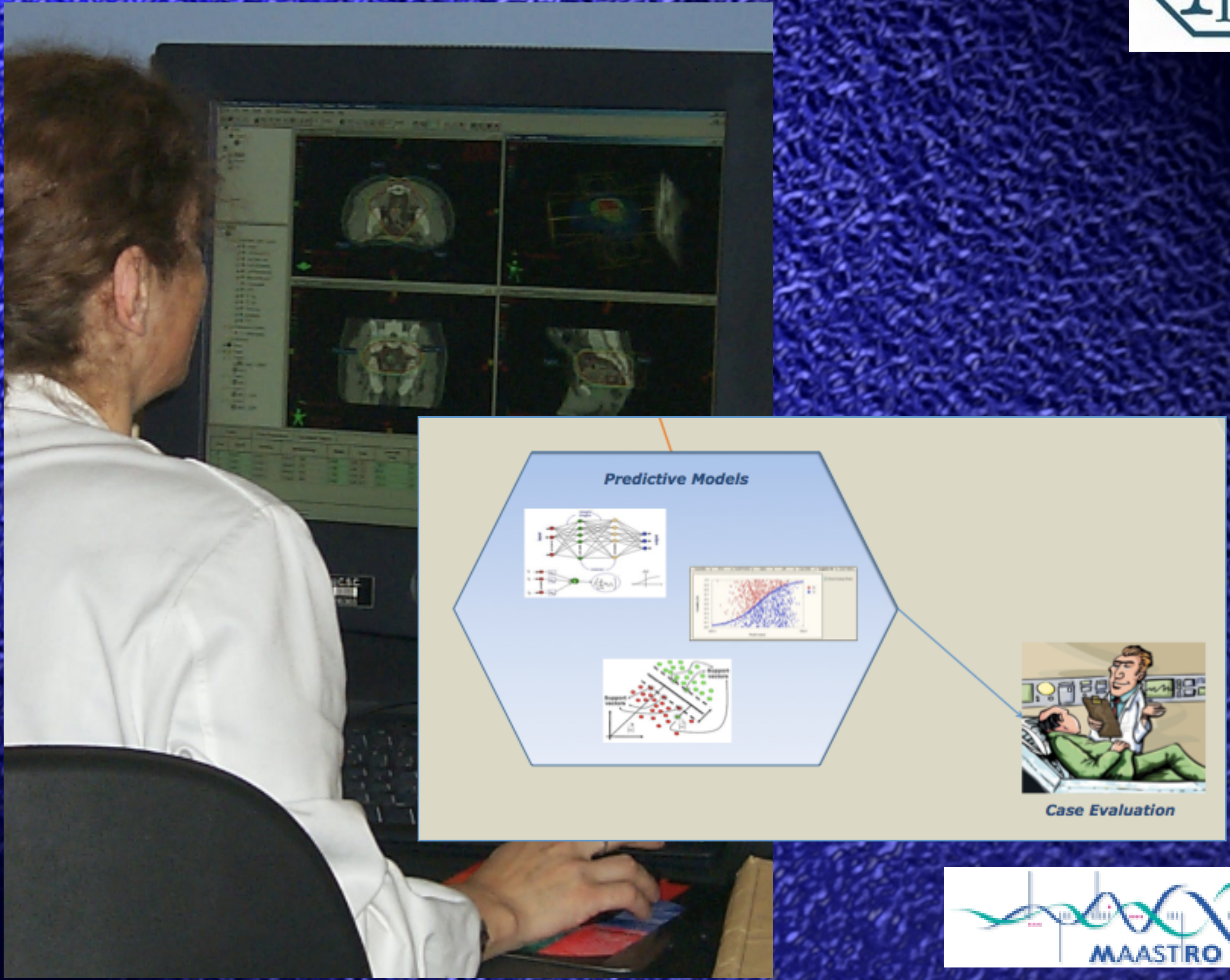
Reti Bayesiane e Support vector machines

Creazione di modelli predittivi

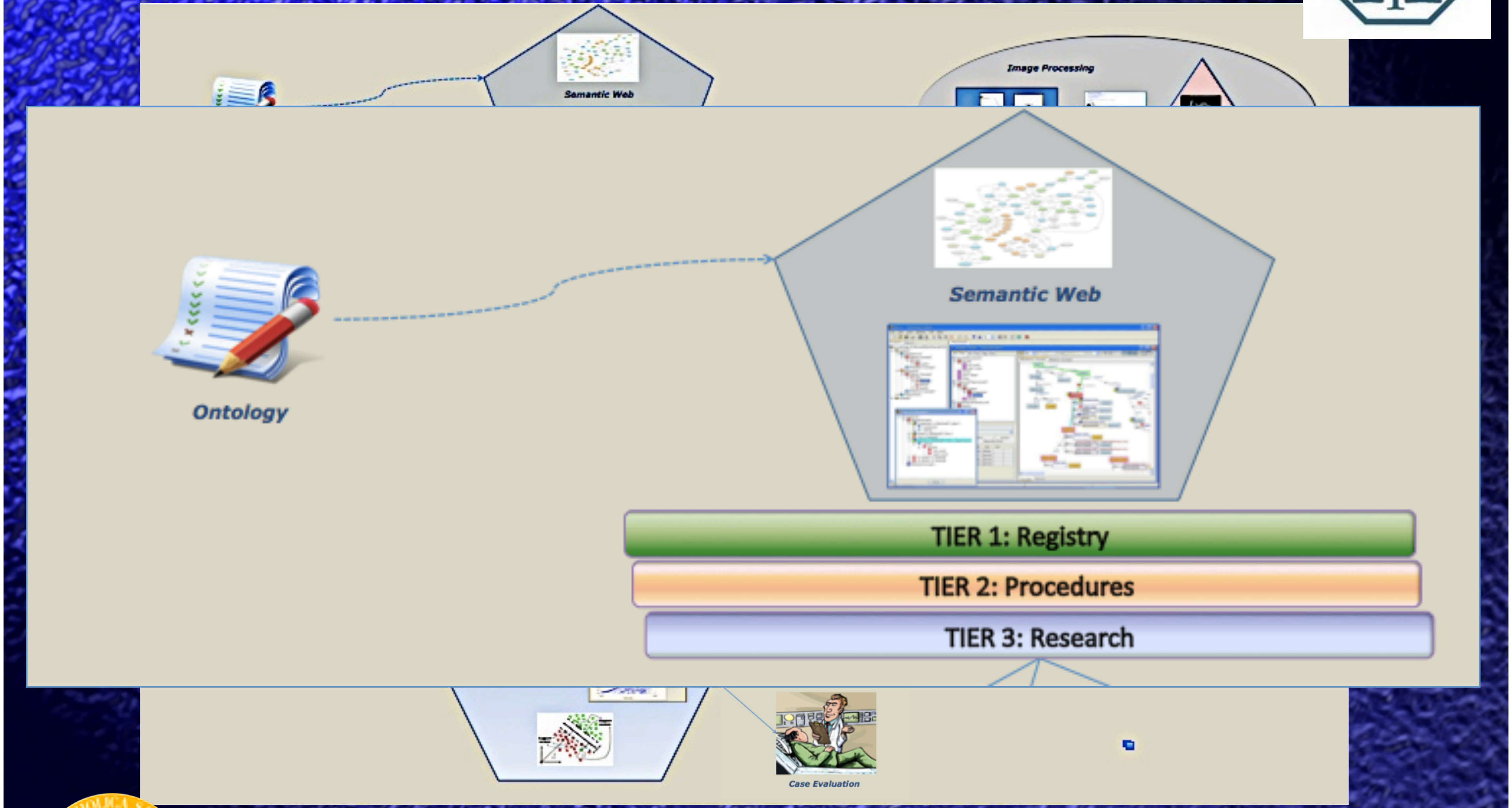
VATE Project

VAlidation
of high TEchnology
based on
large data base
analysis
by learning machine

VATE Project aim


Predictive Models
Case Evaluation

VATE Project aim


Semantic Web
Image Processing
Ontology
Semantic Web
Case Evaluation

TIER 1: Registry

TIER 2: Procedures

TIER 3: Research

SEMANTIC STEP

Variable	*Reference*	*Published code system*
Rectal cancer	*According to the ICD-9 classification*	http://www.icd9data.com/2013/Volume1/140-239/150-159/154/default.htm
Gender	*Male/Female*	http://bioportal.bioontology.org/ontologies/ADW/?p=classes&conceptid=http%3A%2F%2Fwww.owl-ontologies.com%2Funnamed.owl%23Sex
T stage	*According to the TNM staging system*	http://bioportal.bioontology.org/ontologies/NCIT/?p=classes&conceptid=http%3A%2F%2Fncicb.nci.nih.gov%2Fxml%2Fowl%2FEVS%2FThesaurus.owl%23C48885
N stage	*According to the TNM staging system*	http://bioportal.bioontology.org/ontologies/NCIT/?p=classes&conceptid=http%3A%2F%2Fncicb.nci.nih.gov%2Fxml%2Fowl%2FEVS%2FThesaurus.owl%23C48884
…..		http://

ONTOLOGIA

Definizione: deriva dal greco

ὄντος (òntos) = pp del verbo εἰμὶ (eimi) – essere

λόγος (lògos) = discorso, studio, scienza

Formalmente intesa come conoscenza di un insieme di variabili riguardanti un argomento, rappresenta una sorta di dizionario che standardizza terminologie mediche e tecniche di trattamento.

ONTOLOGIA TUMORE DEL RETTO

- 209 variabili analizzate:
  - Registry level: variabili paziente correlate

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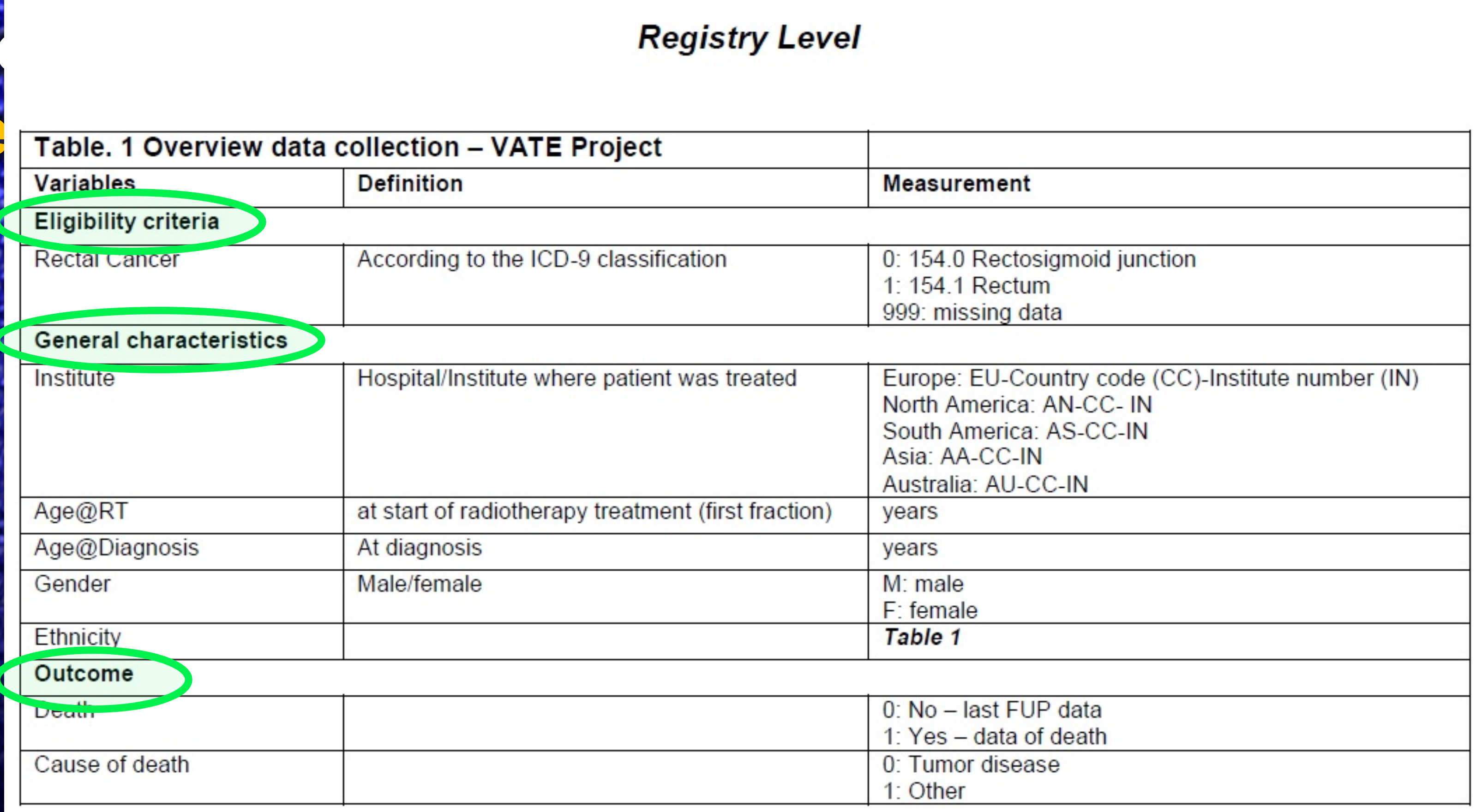
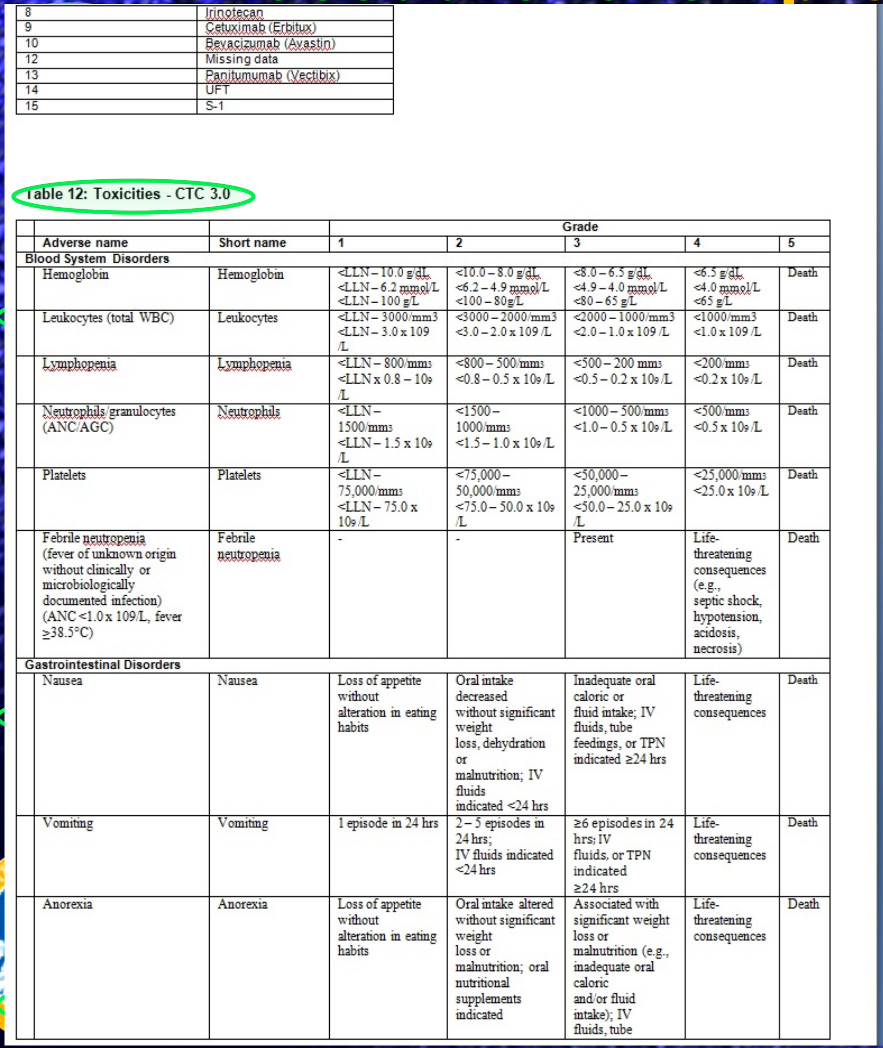


Registry Level

Table. 1 Overview data collection – VATE Project		
Variables	**Definition**	**Measurement**
Eligibility criteria		
Rectal Cancer	According to the ICD-9 classification	0: 154.0 Rectosigmoid junction 1: 154.1 Rectum 999: missing data
General characteristics		
Institute	Hospital/Institute where patient was treated	Europe: EU-Country code (CC)-Institute number (IN) North America: AN-CC- IN South America: AS-CC-IN Asia: AA-CC-IN Australia: AU-CC-IN
Age@RT	at start of radiotherapy treatment (first fraction)	years
Age@Diagnosis	At diagnosis	years
Gender	Male/female	M: male F: female
Ethnicity		***Table 1***
Outcome		
Death		0: No – last FUP data 1: Yes – data of death
Cause of death		0: Tumor disease 1: Other

ONTOLOGIA TUMORE DEL RETTO

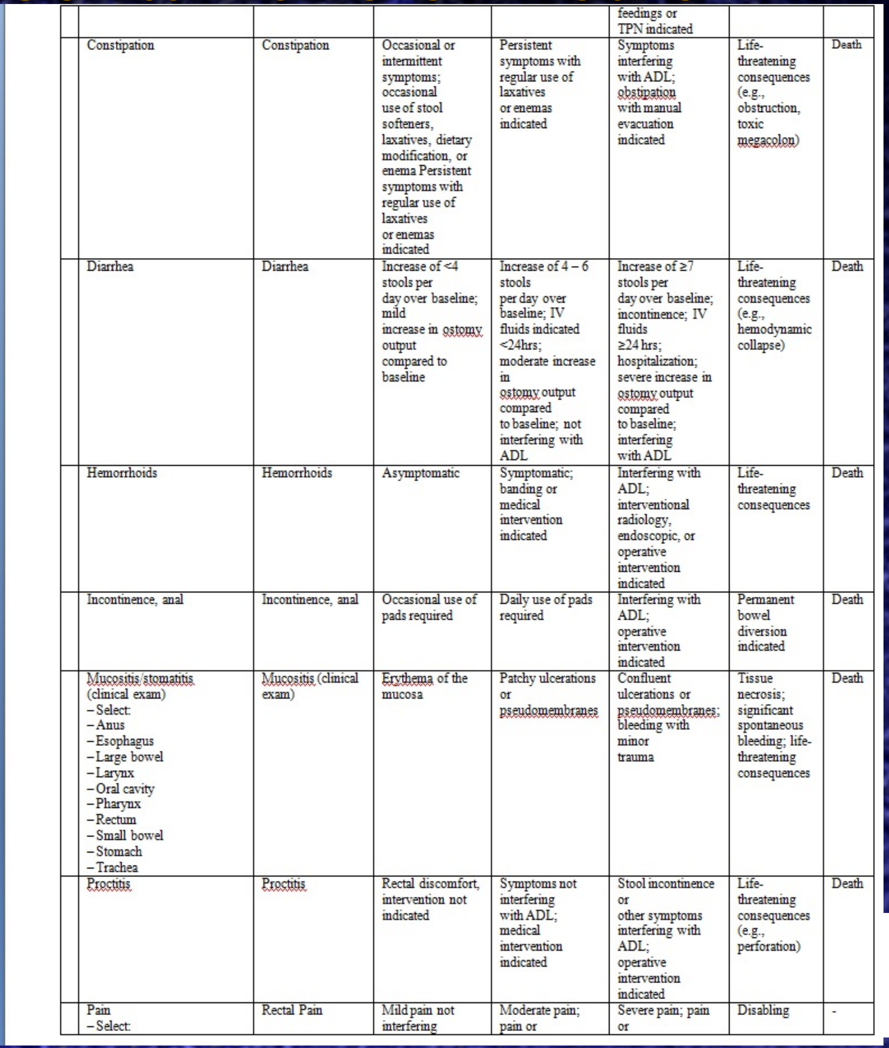
- **209 variabili analizzate:**
  - Procedure level: presentazione clinica e



8	Irinotecan
9	Cetuximab (Erbitux)
10	Bevacizumab (Avastin)
12	Missing data
13	Panitumumab (Vectibix)
14	UFT
15	S-1

Table 12: Toxicities - CTC 3.0

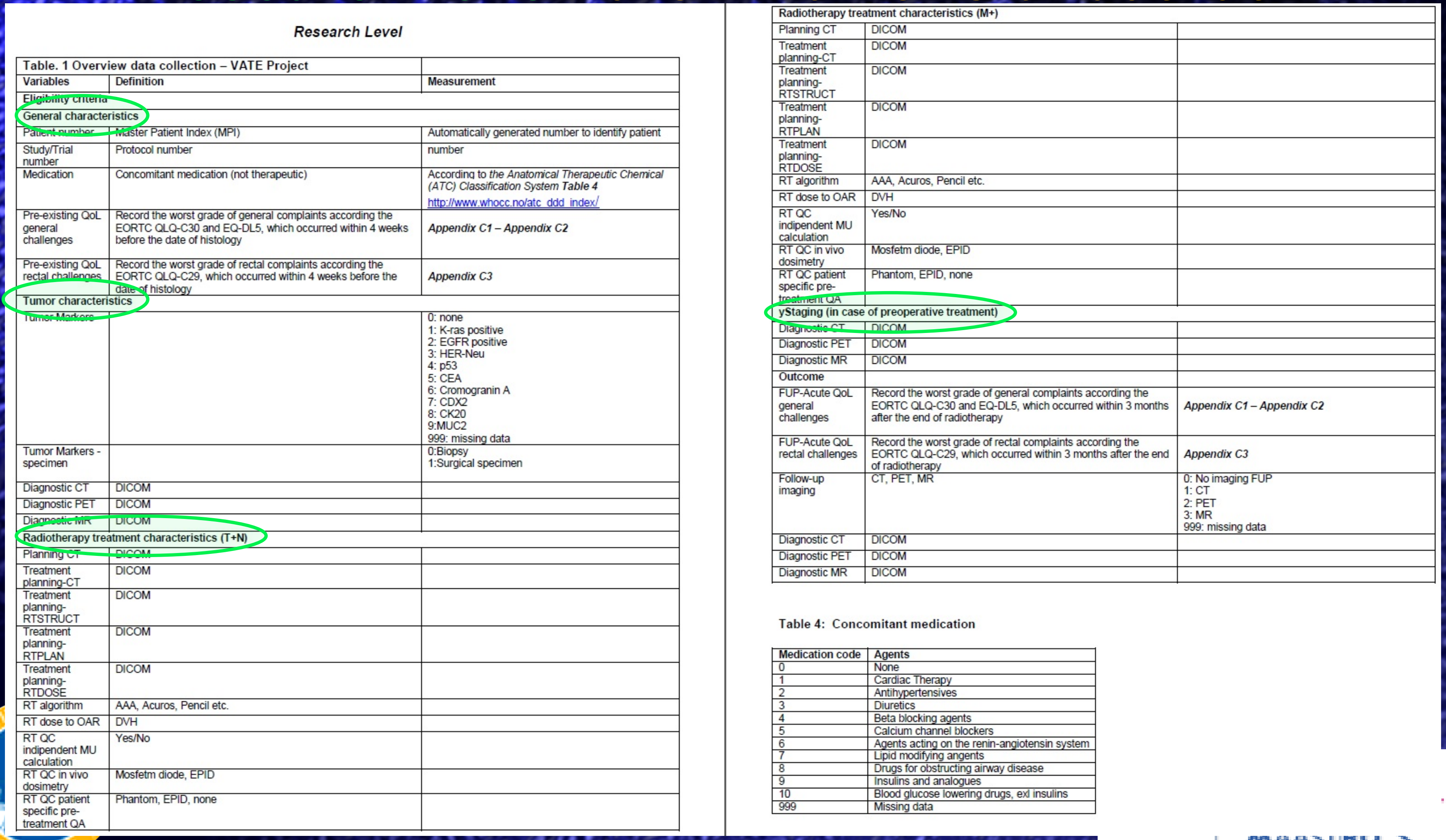
			Grade				
	Adverse name	**Short name**	**1**	**2**	**3**	**4**	**5**
Blood System Disorders							
	Hemoglobin	Hemoglobin	<LLN – 10.0 g/dL <LLN – 6.2 mmol/L <LLN – 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80 – 65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
	Leukocytes (total WBC)	Leukocytes	<LLN – 3000/mm3 <LLN – 3.0 x 109 /L	<3000 – 2000/mm3 <3.0 – 2.0 x 109 /L	<2000 – 1000/mm3 <2.0 – 1.0 x 109 /L	<1000/mm3 <1.0 x 109 /L	Death
	Lymphopenia	Lymphopenia	<LLN – 800/mm3 <LLN x 0.8 – 109 /L	<800 – 500/mm3 <0.8 – 0.5 x 109 /L	<500 – 200 mm3 <0.5 – 0.2 x 109 /L	<200/mm3 <0.2 x 109 /L	Death
	Neutrophils/granulocytes (ANC/AGC)	Neutrophils	<LLN – 1500/mm3 <LLN – 1.5 x 109 /L	<1500 – 1000/mm3 <1.5 – 1.0 x 109 /L	<1000 – 500/mm3 <1.0 – 0.5 x 109 /L	<500/mm3 <0.5 x 109 /L	Death
	Platelets	Platelets	<LLN – 75,000/mm3 <LLN – 75.0 x 109 /L	<75,000 – 50,000/mm3 <75.0 – 50.0 x 109 /L	<50,000 – 25,000/mm3 <50.0 – 25.0 x 109 /L	<25,000/mm3 <25.0 x 109 /L	Death
	Febrile neutropenia (fever of unknown origin without clinically or microbiologically documented infection) (ANC <1.0 x 109/L, fever ≥38.5°C)	Febrile neutropenia	-	-	Present	Life-threatening consequences (e.g., septic shock, hypotension, acidosis, necrosis)	Death
Gastrointestinal Disorders							
	Nausea	Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition; IV fluids indicated <24 hrs	Inadequate oral caloric or fluid intake; IV fluids, tube feedings, or TPN indicated ≥24 hrs	Life-threatening consequences	Death
	Vomiting	Vomiting	1 episode in 24 hrs	2 – 5 episodes in 24 hrs; IV fluids indicated <24 hrs	≥6 episodes in 24 hrs; IV fluids, or TPN indicated ≥24 hrs	Life-threatening consequences	Death
	Anorexia	Anorexia	Loss of appetite without alteration in eating habits	Oral intake altered without significant weight loss or malnutrition; oral nutritional supplements indicated	Associated with significant weight loss or malnutrition (e.g., inadequate oral caloric and/or fluid intake); IV fluids, tube	Life-threatening consequences	Death



					feedings or TPN indicated		
	Constipation	Constipation	Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema Persistent symptoms with regular use of laxatives or enemas indicated	Persistent symptoms with regular use of laxatives or enemas indicated	Symptoms interfering with ADL; obstipation with manual evacuation indicated	Life-threatening consequences (e.g., obstruction, toxic megacolon)	Death
	Diarrhea	Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 – 6 stools per day over baseline; IV fluids indicated <24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL	Increase of ≥7 stools per day over baseline; incontinence; IV fluids ≥24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL	Life-threatening consequences (e.g., hemodynamic collapse)	Death
	Hemorrhoids	Hemorrhoids	Asymptomatic	Symptomatic; banding or medical intervention indicated	Interfering with ADL; interventional radiology, endoscopic, or operative intervention indicated	Life-threatening consequences	Death
	Incontinence, anal	Incontinence, anal	Occasional use of pads required	Daily use of pads required	Interfering with ADL; operative intervention indicated	Permanent bowel diversion indicated	Death
	Mucositis/stomatitis (clinical exam) – Select: – Anus – Esophagus – Large bowel – Larynx – Oral cavity – Pharynx – Rectum – Small bowel – Stomach – Trachea	Mucositis (clinical exam)	Erythema of the mucosa	Patchy ulcerations or pseudomembranes	Confluent ulcerations or pseudomembranes; bleeding with minor trauma	Tissue necrosis; significant spontaneous bleeding; life-threatening consequences	Death
	Proctitis	Proctitis	Rectal discomfort, intervention not indicated	Symptoms not interfering with ADL; medical intervention indicated	Stool incontinence or other symptoms interfering with ADL; operative intervention indicated	Life-threatening consequences (e.g., perforation)	Death
	Pain – Select:	Rectal Pain	Mild pain not interfering	Moderate pain; pain or	Severe pain; pain or	Disabling	-

ONTOLOGIA TUMORE DEL RETTO

- **209 variabili analizzate:**
  - Research level: archiviazione di dati utili



Research Level

Table. 1 Overview data collection – VATE Project		
Variables	**Definition**	**Measurement**
Eligibility criteria		
General characteristics		
Patient number	Master Patient Index (MPI)	Automatically generated number to identify patient
Study/Trial number	Protocol number	number
Medication	Concomitant medication (not therapeutic)	According to *the Anatomical Therapeutic Chemical (ATC) Classification System* ***Table 4*** http://www.whocc.no/atc_ddd_index/
Pre-existing QoL general challenges	Record the worst grade of general complaints according the EORTC QLQ-C30 and EQ-DL5, which occurred within 4 weeks before the date of histology	***Appendix C1 – Appendix C2***
Pre-existing QoL rectal challenges	Record the worst grade of rectal complaints according the EORTC QLQ-C29, which occurred within 4 weeks before the date of histology	***Appendix C3***
Tumor characteristics		
Tumor Markers		0: none 1: K-ras positive 2: EGFR positive 3: HER-Neu 4: p53 5: CEA 6: Cromogranin A 7: CDX2 8: CK20 9:MUC2 999: missing data
Tumor Markers - specimen		0:Biopsy 1:Surgical specimen
Diagnostic CT	DICOM	
Diagnostic PET	DICOM	
Diagnostic MR	DICOM	
Radiotherapy treatment characteristics (T+N)		
Planning CT	DICOM	
Treatment planning-CT	DICOM	
Treatment planning-RTSTRUCT	DICOM	
Treatment planning-RTPLAN	DICOM	
Treatment planning-RTDOSE	DICOM	
RT algorithm	AAA, Acuros, Pencil etc.	
RT dose to OAR	DVH	
RT QC indipendent MU calculation	Yes/No	
RT QC in vivo dosimetry	Mosfetm diode, EPID	
RT QC patient specific pre-treatment QA	Phantom, EPID, none	
Radiotherapy treatment characteristics (M+)		
Planning CT	DICOM	
Treatment planning-CT	DICOM	
Treatment planning-RTSTRUCT	DICOM	
Treatment planning-RTPLAN	DICOM	
Treatment planning-RTDOSE	DICOM	
RT algorithm	AAA, Acuros, Pencil etc.	
RT dose to OAR	DVH	
RT QC indipendent MU calculation	Yes/No	
RT QC in vivo dosimetry	Mosfetm diode, EPID	
RT QC patient specific pre-treatment QA	Phantom, EPID, none	
yStaging (in case of preoperative treatment)		
Diagnostic CT	DICOM	
Diagnostic PET	DICOM	
Diagnostic MR	DICOM	
Outcome		
FUP-Acute QoL general challenges	Record the worst grade of general complaints according the EORTC QLQ-C30 and EQ-DL5, which occurred within 3 months after the end of radiotherapy	***Appendix C1 – Appendix C2***
FUP-Acute QoL rectal challenges	Record the worst grade of rectal complaints according the EORTC QLQ-C29, which occurred within 3 months after the end of radiotherapy	***Appendix C3***
Follow-up imaging	CT, PET, MR	0: No imaging FUP 1: CT 2: PET 3: MR 999: missing data
Diagnostic CT	DICOM	
Diagnostic PET	DICOM	
Diagnostic MR	DICOM	

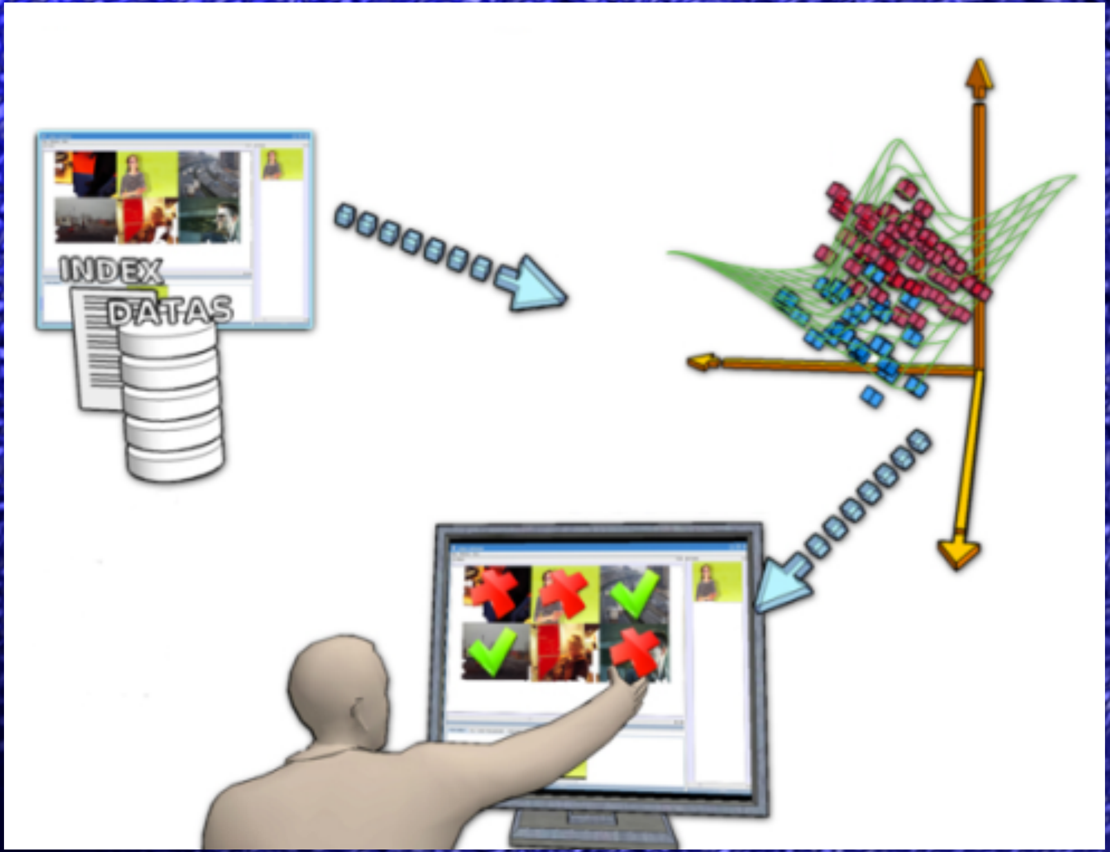
Table 4: Concomitant medication

Medication code	Agents
0	None
1	Cardiac Therapy
2	Antihypertensives
3	Diuretics
4	Beta blocking agents
5	Calcium channel blockers
6	Agents acting on the renin-angiotensin system
7	Lipid modifying angents
8	Drugs for obstructing airway disease
9	Insulins and analogues
10	Blood glucose lowering drugs, exl insulins
999	Missing data

LARGE DATABASE

LARGE
DATABASE

DATA MINING


INDEX
DATAS

- *Reti Bayesiane*
- *Support vector machines*

OBIETTIVI 1

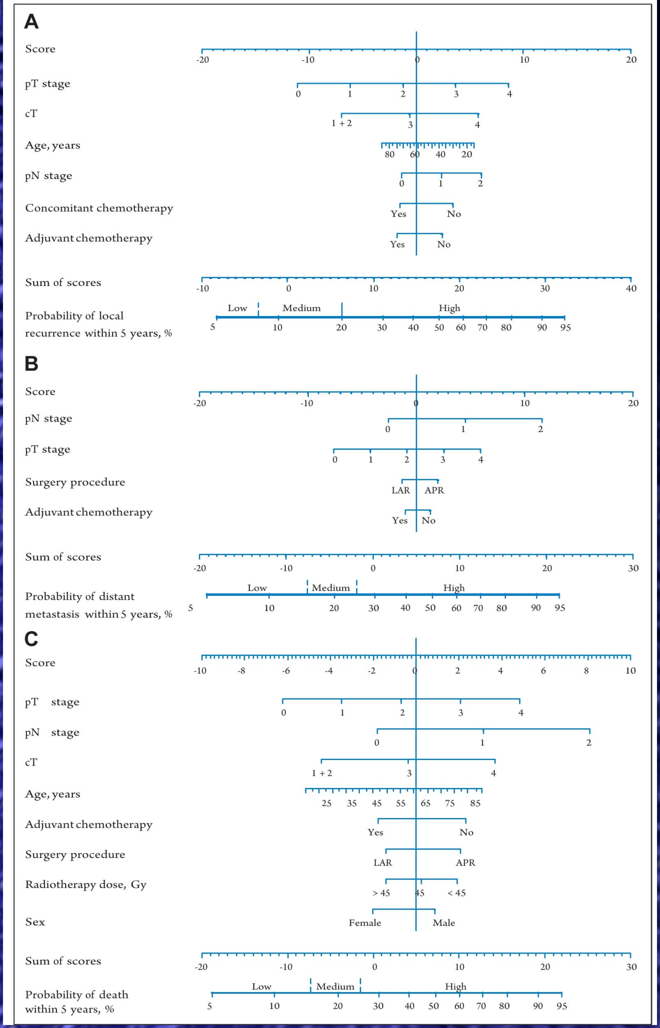
Calibrare i vari fattori analizzati al fine di **pesare** i risultati di ogni singolo Centro partecipante

Department
Employee
Customer
Sales_Database
ProductCategory

OBIETTIVI 2

Creare modelli predittivi per diversi outcomes (controllo locale, sopravvivenza e complicanze da trattamento)

- Linee terapeutiche personalizzate
- Programmi di follow-up piu' intensi in alcuni casi ben selezionati



J Clin Oncol. 2011 Aug 10;29(23):3163-72.

Acknowledgements

VATE 1.0

Università Cattolica S.Cuore, Rome

- A Damiani
- .N Dinapoli
- MP Gori
- MA Gambacorta
- E Meldolesi
- D Pasini
- L Tagliaferri
- V Valentini (PI)

Maastro Clinic, Maastricht

- A Dekker
- J Van Soest
- P Lambin

Grazie!