

NED-DH FIELD EXPERIENCE (BONE MARROW AND BIOLOGICAL FLUIDS)



DOTT.SSA MARIA LORUBBIO

**DEPARTMENT OF LABORATORY AND TRANSFUSION MEDICINE
OF THE SOUTHEAST TUSCANY LOCAL HEALTH UNIT (USL)**



THE TERRITORY OF THE SOUTHEAST TUSCANY USL

As of 2016 from 12 ASL → 3 ASL (Local Health Authority)

SOUTHEAST TUSCANY USL:

Ex Asl 7 of Siena, 8 of Arezzo, 9 of Grosseto

[Source ISTAT 1/01/2020]

SURFACE AREA: 11.560 Km² ≈ half of the regional area(22.990 km²); (32%) is mountainous, 42% hilly, 26% flat

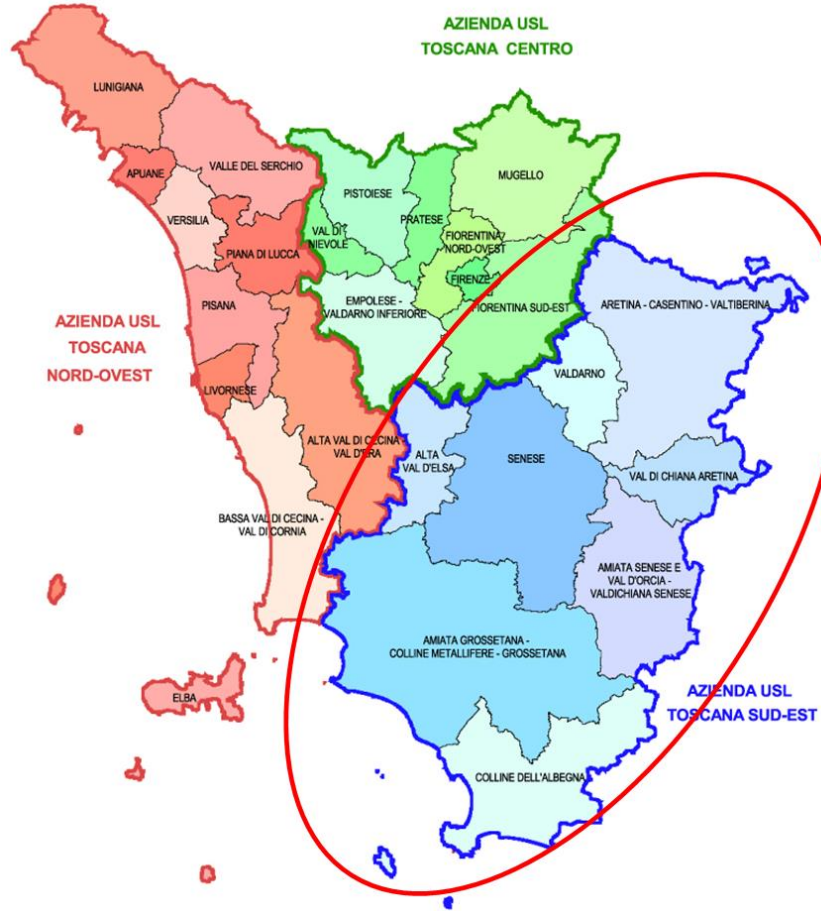
100 municipalities: 39 mountainous, 20 partially mountainous, and 1 island

[Source 01/01/2018]

INHABITANTS: about 833.634 (of which ¼ are over 65 years old): Siena 32% , Arezzo 41% and Grosseto 27%

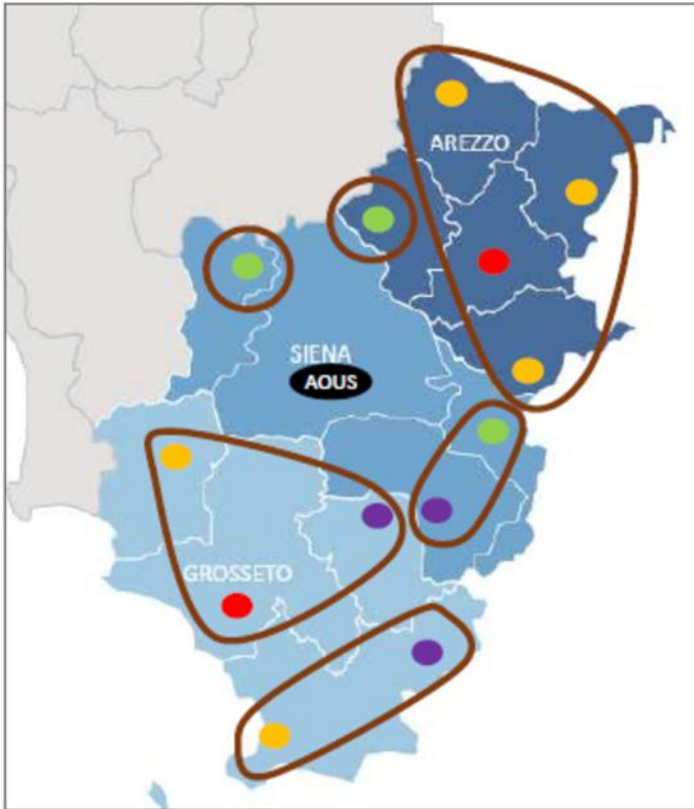
[Source Istat 01/01/2019]

POPULATION DENSITY: 72,50 inhabitants per Km²



THE TERRITORY OF THE SOUTHEAST TUSCANY USL

- 6 Hospital Center
- 13 Hospital Establishments

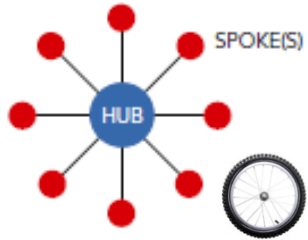


LEGENDA

- Osp di riferimento provinciale
- Osp di riferimento zonale
- Osp di riferimento territoriale
- Osp di Prossimità

Hospital Center	Hospital Establishment	DM70 Classification	AUSL Classification
PO of Aretino, Casentino, Valtiberina and Valdichiana Aretina area	S.O. Arezzo	I Level	Of provincial reference
	S.O. Bibbiena	Distressed Areas	Of territorial reference
	S.O. San Sepolcro	Distressed Areas	Of territorial reference
	S.O. Cortona	Base	Of territorial reference
PO of Valdarno	Montevarchi	I Level	Of zonal reference
PO of Alta Val d'Elsa	Poggibonsi	Base	Of zonal reference
PO of Amiata Senese, Val d'Orcia, Valdichiana Senese	S.O. Montepulciano	Base	Of zonal reference
	S.O. Abbadia San Salvatore	Distressed Areas	Of proximity
PO of Amiata Grossetana, Metallifere Hills, Grossetana	S.O. Grosseto	I Level	Of provincial reference
	S.O. Massa Marittima	Base	Of territorial reference
	S.O. Castel del Piano	Distressed Areas	Of proximity
PO of Albegna Hills	S.O. Orbetello	Base	Of territorial reference
	S.O. Pitigliano	Distressed Areas	Of proximity

ORGANIZATION MODEL OF THE SOUTHEAST TUSCANY USL



PO of Amiata Grossetana, Metallifere Hills, Grossetana

PO of Alta Val d'Elsa



S.O. Castel del Piano



S.O. Grosseto



S.O. Massa Marittima



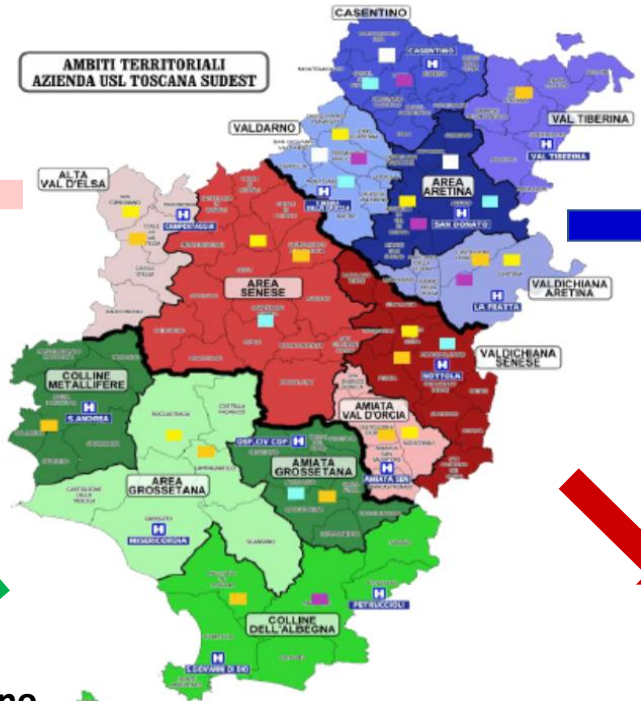
S.O. Orbetello



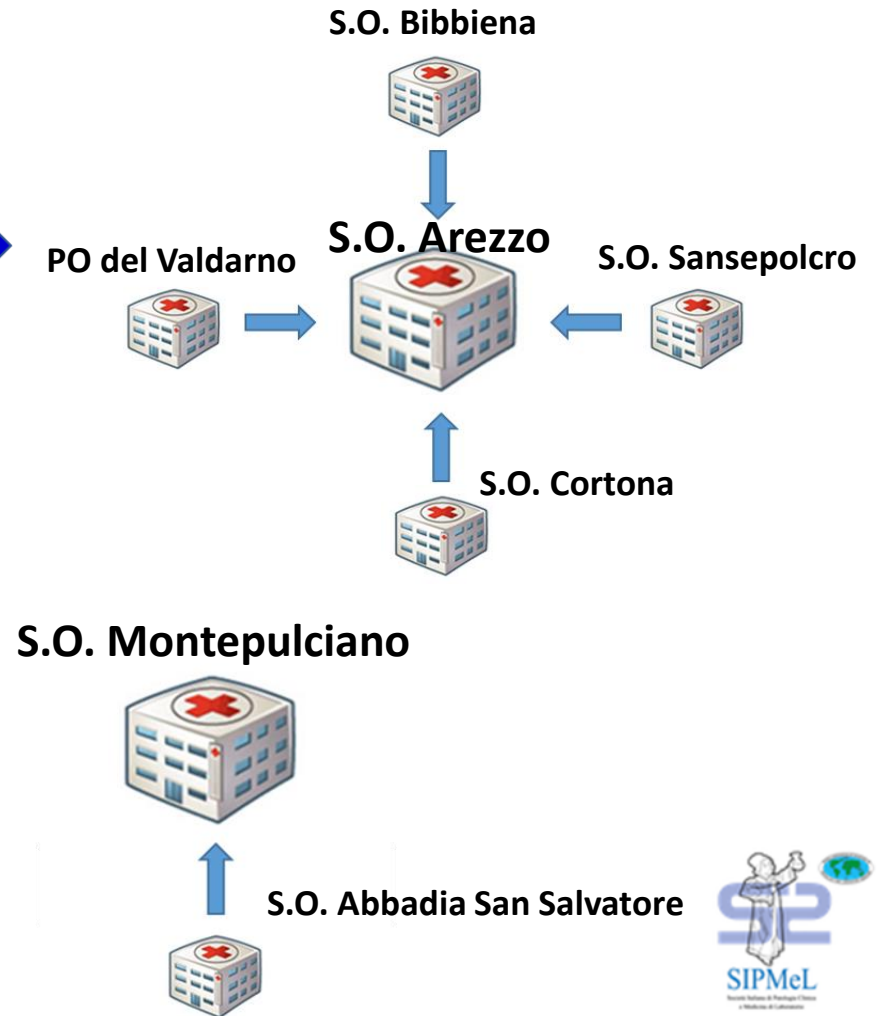
S.O. Pitigliano



PO of Albegna Hills



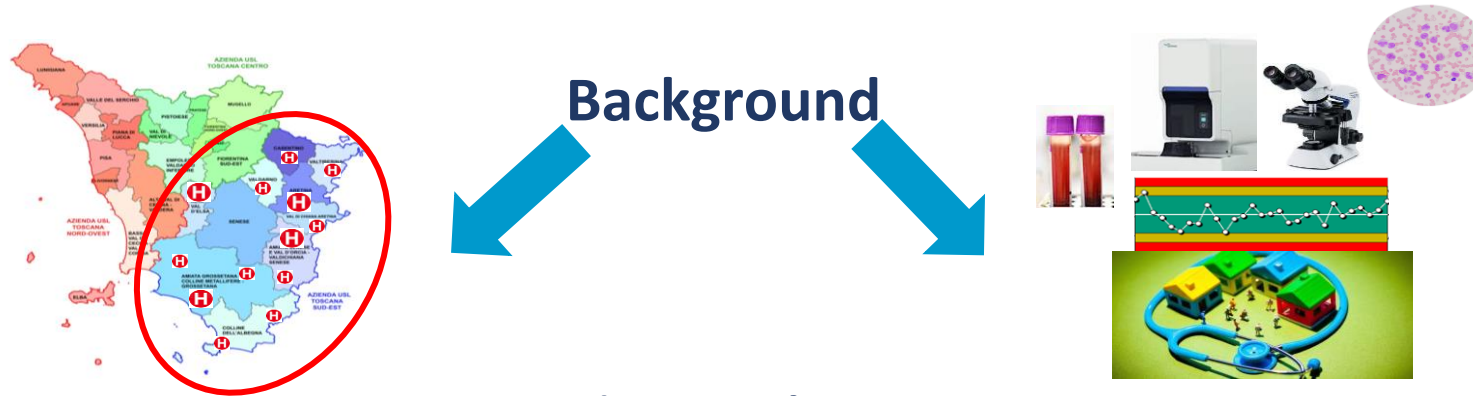
Routine samples (from CP and S.O.) are transported to 4°C in between 2-4 hours



PROJECT

LABORATORY TELEMEDICINE: THE HAEMATOLOGY NETWORK OF THE SOUTHEAST TUSCANY USL

DEPARTMENT OF LABORATORY AND TRANSFUSION MEDICINE



DE GRUYTER

Clin Chem Lab Med 2021; 59(6): 1035–1045

Opinion Paper

Mario Plebani*

Laboratory medicine in the COVID-19 era: six lessons for the future



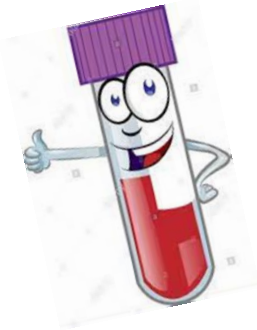
SIX MISSIONS

1. Digitalization, Innovation, Competitiveness, and Culture;
2. Green Revolution and Ecological Transition;
3. Infrastructures for Sustainable Mobility;
4. Education and Research;
5. Inclusion and Cohesion;
6. Health.

PROJECT

LABORATORY TELEMEDICINE: THE HAEMATOLOGY NETWORK OF THE SOUTHEAST TUSCANY USL

Objectives and Purpose



The purpose of the project is to provide a complete blood count test and the appropriate in-depth analysis with a network organization, implementing an innovative "Distributed" laboratory organizational model that is uniform and widespread in the quality of service.



✓ PRIMARY OBJECTIVE

Realization and implementation of a decentralized analytical network that transmits data, graphs, and cellular images shareable among the 12 laboratories of the network.

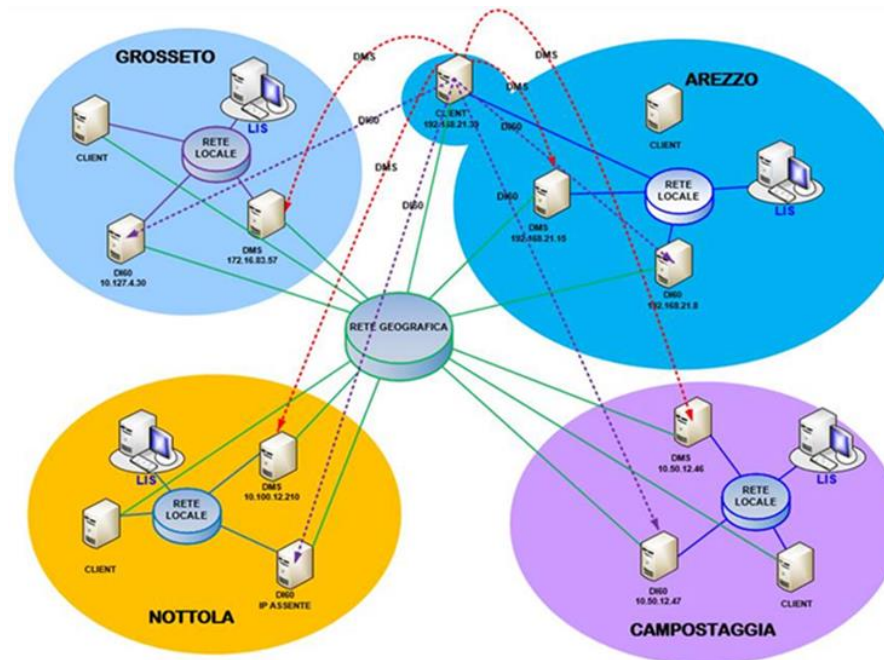
✓ SECONDARY OBJECTIVE

1. Connect all laboratories (Hub and Spoke) so that all samples from the territorial districts are processed in each peripheral laboratory, without sample movement.
2. Teleconsultation and telecooperation, consultation and discussion of clinical cases with other professionals in the network, sharing data, images, and graphs in a "Distributed Team" approach.
3. Continuity of care and patient monitoring with consistent analytical quality standards.
4. Training of laboratory professionals: maintaining competencies through collegial review (peer review) of complicated clinical cases and difficult diagnoses; training for new hires.

PROJECT

LABORATORY TELEMEDICINE: THE HAEMATOLOGY NETWORK OF THE SOUTHEAST TUSCANY USL

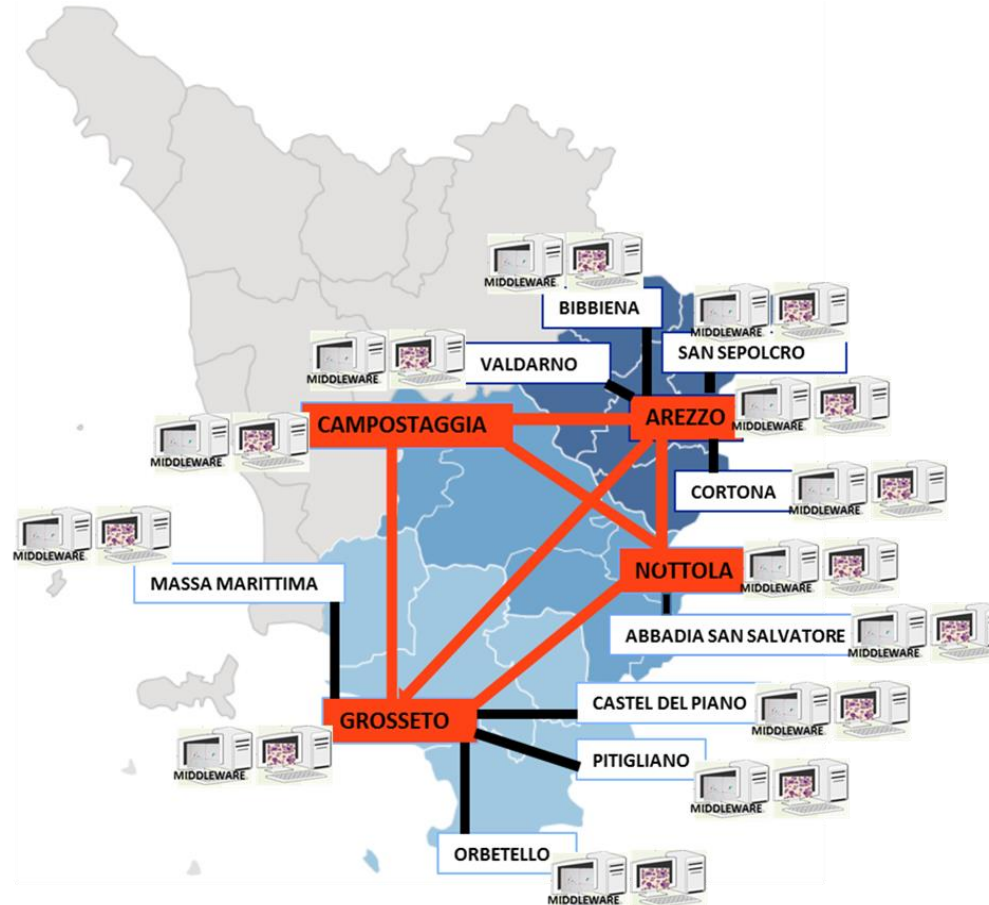
1. CORPORATE IT INFRASTRUCTURE NETWORK (Information and Communication Technologies →ICT's)
2. INSTRUMENTAL EQUIPMENT AND WEB APPLICATIONS NEEDED TO TRANSMIT DATA, LABORATORY HEMATOLOGY GRAPHS, AND DIGITAL CELLULAR IMAGES SHAREABLE AMONG ALL LABORATORIES IN THE NETWORK
3. REDEFINITION OF FLOWS
4. STAFF TRAINING



PROJECT

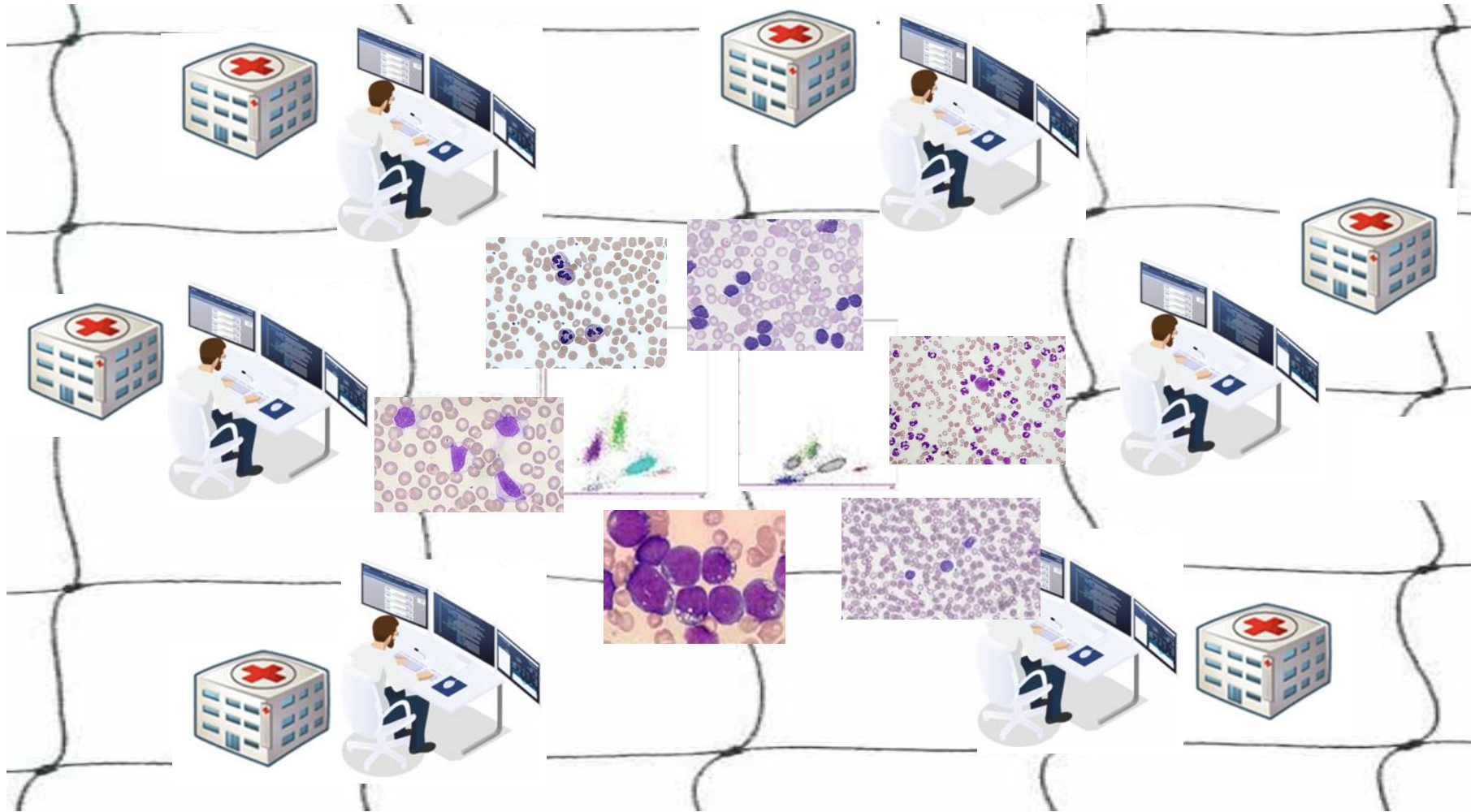
LABORATORY TELEMEDICINE: THE HAEMATOLOGY NETWORK OF THE SOUTHEAST TUSCANY USL

The state of the art



PROJECT

LABORATORY TELEMEDICINE: THE HAEMATOLOGY NETWORK OF THE SOUTHEAST TUSCANY USL



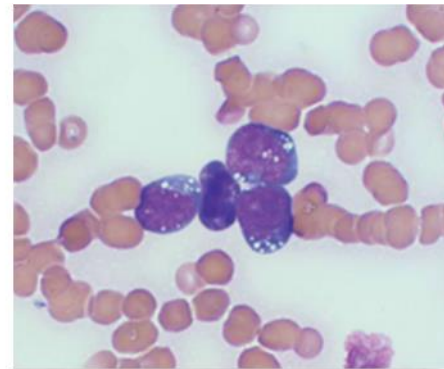
PROJECT

LABORATORY TELEMEDICINE: THE HAEMATOLOGY NETWORK OF THE SOUTHEAST TUSCANY USL

TELECONSULTATION

The reorganization of laboratory
diagnostics and imaging
diagnostics:

The significant economic and organizational impact of the initiatives for the development of the laboratory diagnostics sector (including advanced diagnostic techniques) and imaging diagnostics has made it essential to implement initiatives aimed, among other things, at ensuring the interoperability of hospital and ASL (local health authority) systems (both intra- and inter-regional), with particular reference to teleconsultation (second opinion).



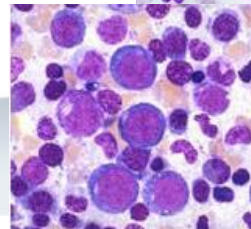
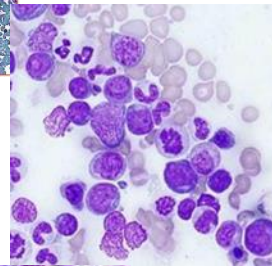
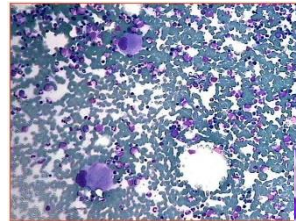
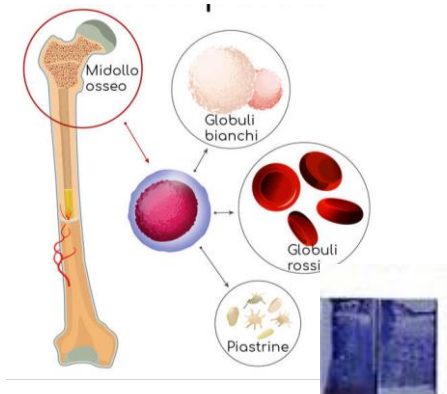
TOWARDS NEW HORIZONS ...



PROJECT

LABORATORY TELEMEDICINE: THE HAEMATOLOGY NETWORK OF THE SOUTHEAST TUSCANY USL

HEALTH TELECOOPERATION: SHARING OF BONE MARROW ASPIRATE IMAGES WITH CLINICAL HEMATOLOGY



LABORATORY TELEMEDICINE: THE HAEMATOLOGY NETWORK OF THE SOUTHEAST TUSCANY USL

HEALTHCARE TELECOOPERATION: REMOTE SHARING AND MANAGEMENT OF BONE MARROW ASPIRATE IMAGES WITH CLINICAL HEMATOLOGY

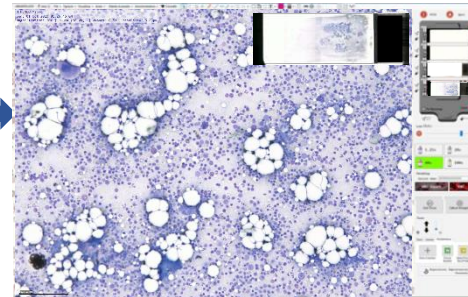
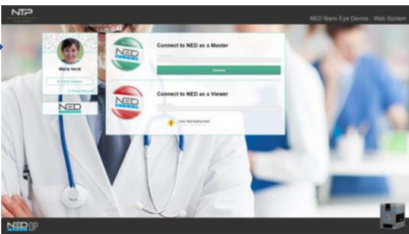
WORKFLOW PROPOSAL



The bone marrow slides stained and prepared by the laboratory are placed in the designated slots of the digital microscopy



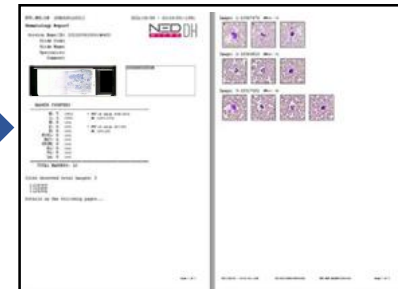
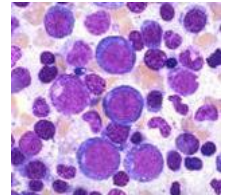
Sharing the session with the clinical hematologist with full remote management, objective change (1.25x, 20x, 40x, 100x), focusing of microscopic fields



Creation of the slide minimap



Shared evaluation of the bone marrow smear by the clinical hematologist at 20x and 40x for the bone marrow aspirate, observation at 100x with the possibility of saving images of microscopic fields



Reporting

LABORATORY TELEMEDICINE: THE HAEMATOLOGY NETWORK OF THE SOUTHEAST TUSCANY USL

**INSTRUMENTAL EVALUATION OF BONE MARROW ASPIRATE SMEAR
NED-DH VERSUS MANUAL MICROSCOPY**

Materials and Methods



- **44 patients from the Clinical Hematology Department of San Donato Hospital Arezzo with Bone Marrow Aspirate**
- **2 slides with May-Grunwald Giemsa panoptic staining for each patient**
- **Evaluation and counting of 500 cells by 2 experienced operators for reading on NED-DH digital microscope and manual microscope (3rd operator in case of disagreement between the 2 operators)**

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The Official journal of the International Society for Laboratory Hematology



ICSH guidelines for the standardization of bone marrow specimens and reports

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Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrumental Methods; Approved Standard—Second Edition

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LABORATORY TELEMEDICINE: THE HAEMATOLOGY NETWORK OF THE SOUTHEAST TUSCANY USL

INSTRUMENTAL EVALUATION OF BONE MARROW ASPIRATE SMEAR NED-DH VERSUS MANUAL MICROSCOPY

Materials and Methods

VERIFY

- Agreement in the evaluation of the **QUALITY** of the preparation (10x-20x): poor, good, excellent
- Agreement: Presence/Absence of fragments (10x-20x)
- Agreement in the evaluation of the **CELLULARITY** of the preparation (10x-20x): reduced, normal, increased
- In adequate preparations, comparison **BONE MARROW ASPIRATE (40x, 100x)** by counting 500 cells:

Granulocyte series %

Erythroid series %

Lymphocytes %

Plasma cells %

Blasts %

L/E ratio

Megakaryocytes (10x-20x)

International Journal of Laboratory Hematology

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ICSH guidelines for the standardization of bone marrow specimens and reports

INSTRUMENTAL EVALUATION OF BONE MARROW ASPIRATE SMEAR NED-DH VERSUS MANUAL MICROSCOPY

Materials and Methods

Statistical analysis:

- Cohen's Kappa for qualitative evaluations of the preparation: QUALITY, FRAGMENTS, CELLULARITY
- Passing-Bablok regression analysis and Bland-Altman plot for quantitative comparison of the BONE MARROW ASPIRATE
- ICC (Intraclass Correlation Coefficients) 95% CI

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Vol. 33 No. 11
Replaces EP09-A2-IR
Vol. 30 No. 17

Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Third Edition

Volume 33 Number 11

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Thomas E. Gwise, PhD
Beimar Iriarte, MS
Anders Kallner, MD, PhD
Kristian Linnet, MD, PhD
Robert Magari, PhD
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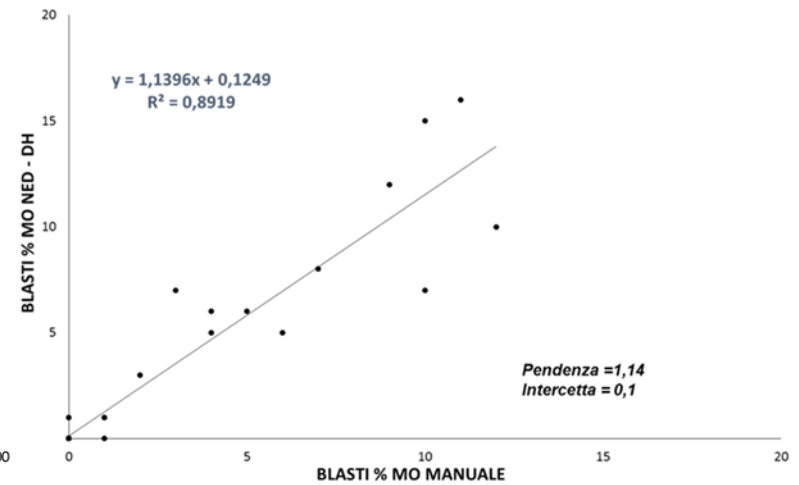
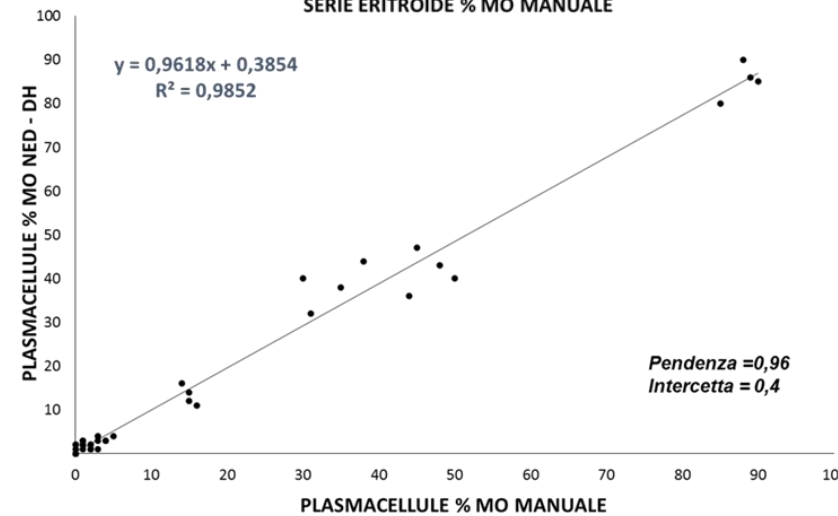
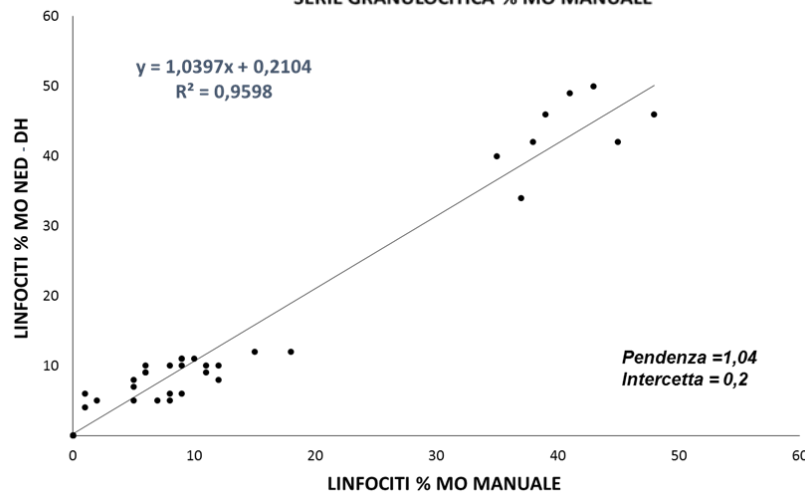
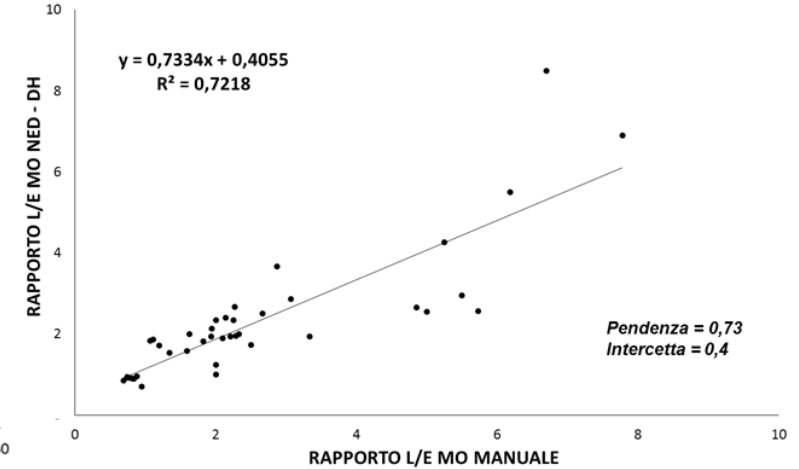
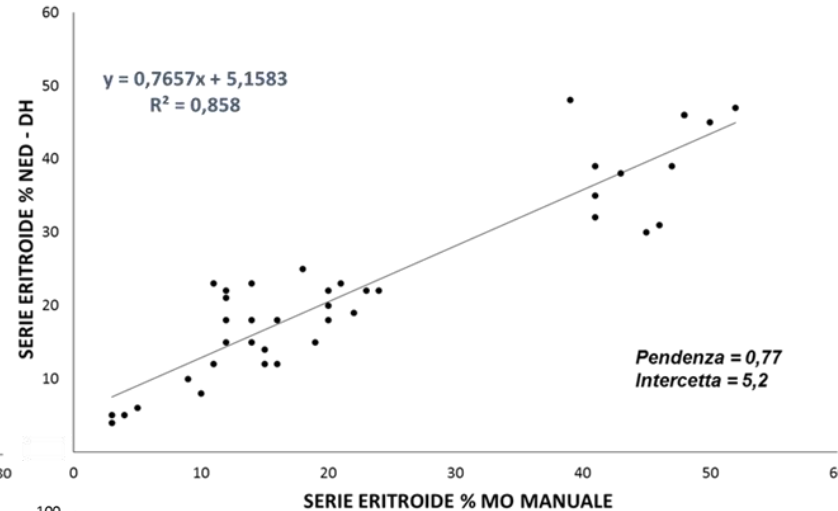
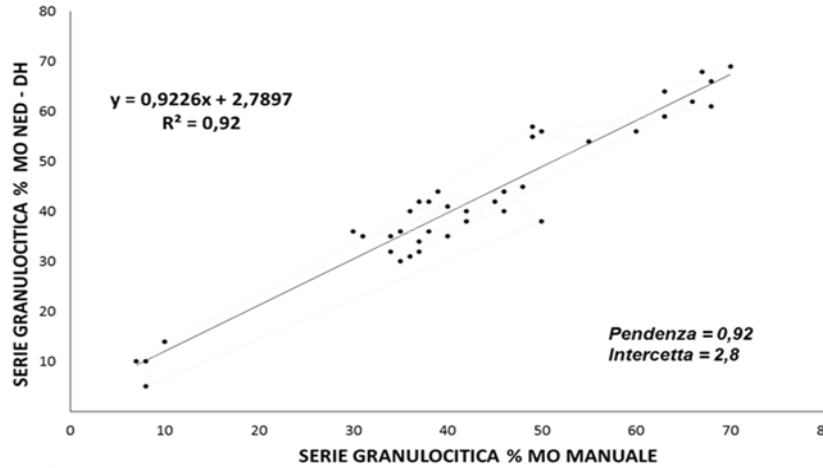


ICSH guidelines for the standardization of bone marrow specimens and reports

INSTRUMENTAL EVALUATION OF BONE MARROW ASPIRATE SMEAR NED-DH VERSUS MANUAL MICROSCOPY

Passing-Bablok regression analysis

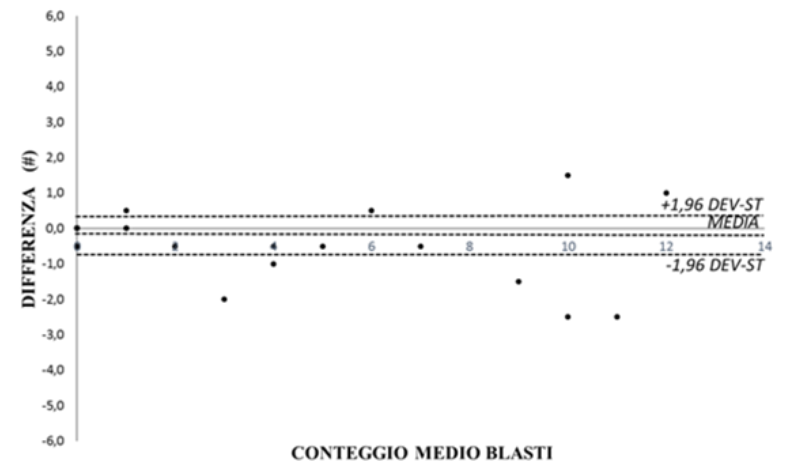
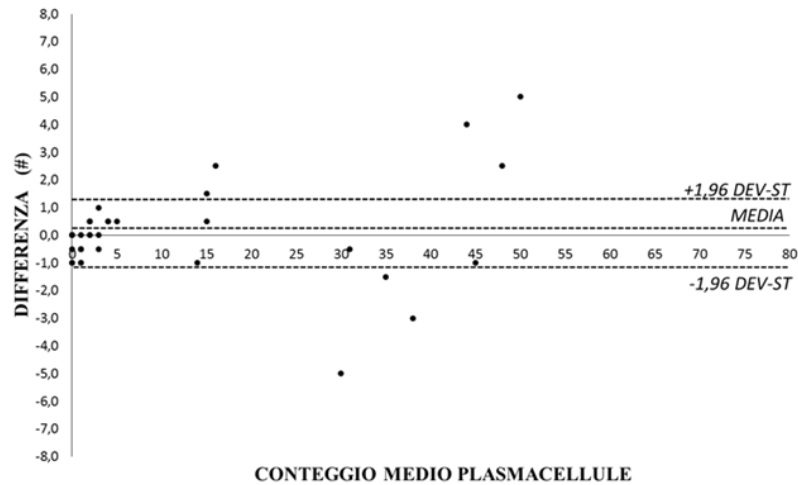
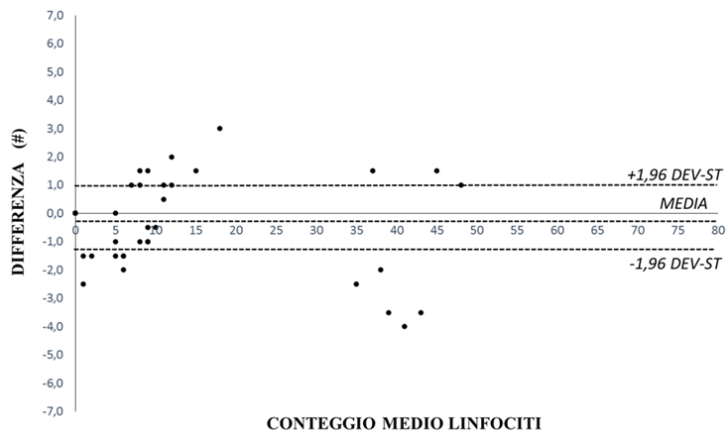
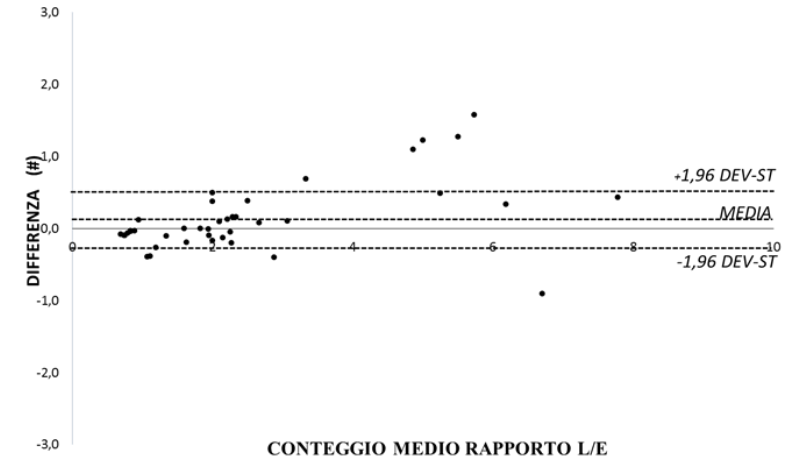
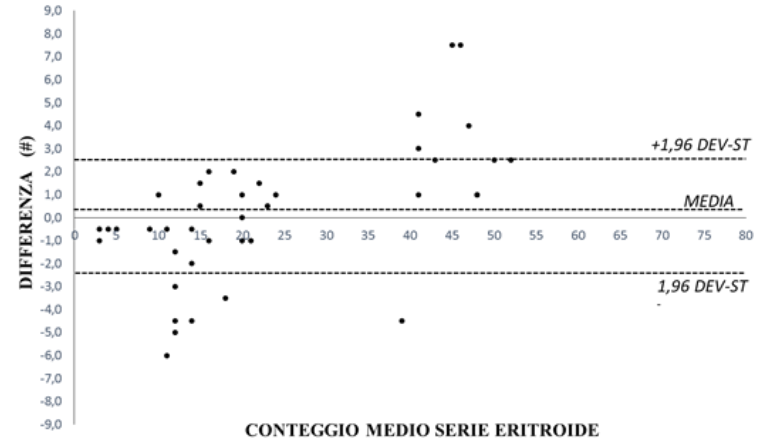
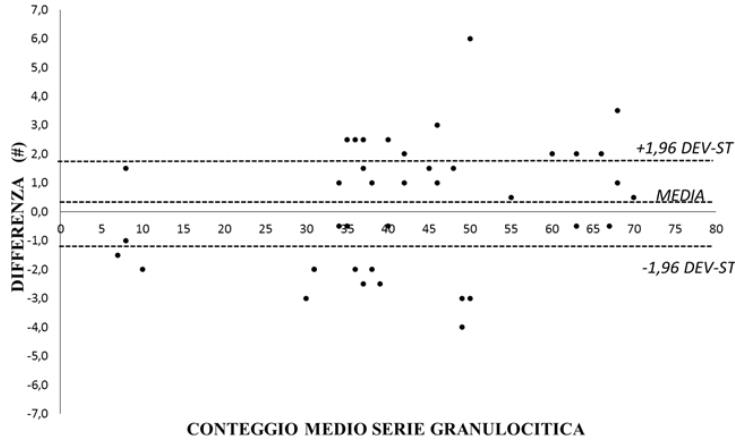
RESULTS



INSTRUMENTAL EVALUATION OF BONE MARROW ASPIRATE SMEAR NED-DH VERSUS MANUAL MICROSCOPY

Bland-Altman plot

RESULTS



Bland-Altman plot

Results

- Cohen's Kappa = 0.85 → Agreement on the QUALITY of the preparation (10x-20x)
- Cohen's Kappa = 0.85 → Agreement: Presence/Absence of fragments (10x-20x)
- Cohen's Kappa = 0.81 → Agreement on the CELLULARITY of the preparation (10x-20x)

Interclass correlation coefficients					
	Interclass correlation	Confidence interval 95%		Test F	
		Lower Limit	Upper Limit	Value	Sig
Granulocyte series	0,981	0,964	0,990	51,985	0,00001
Erythroid series	0,954	0,913	0,975	21,640	0,00001
Leukocyte series	0,989	0,978	0,994	87,454	0,00001
Plasmocyte series	0,996	0,993	0,998	255,468	0,00001
Blast series	0,961	0,926	0,979	25,465	0,00001
Ratio L/E	0,917	0,845	0,956	12,110	0,00001

CLINICAL CASE

53-year-old patient in follow-up for multiple myeloma for 6 years

Blood tests at the last check-up

Creatinine: 3,21 mg/dL (0,67-1,17)

GFR (CKD-EPI): 20,9 mL/min/1,73 mq (≥ 60)

Uric acid: 9,3 mg/dL

Calcium: 17,7* mg/dL

Monoclonal component (Lambda)

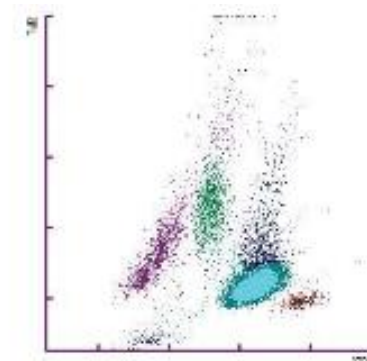
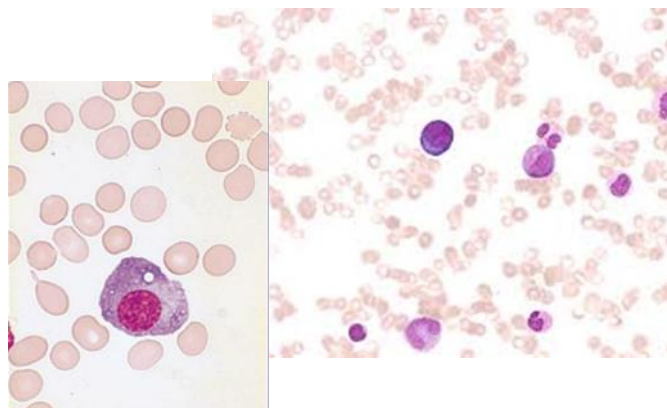
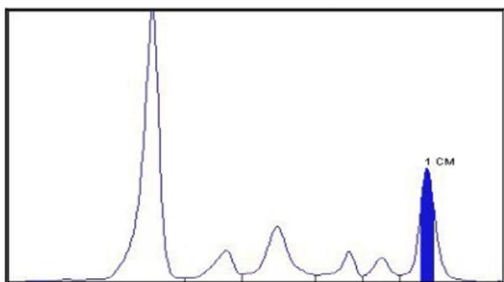
Proteinuria of Bence Jones (Lambda)

COMPLETE BLOOD COUNT

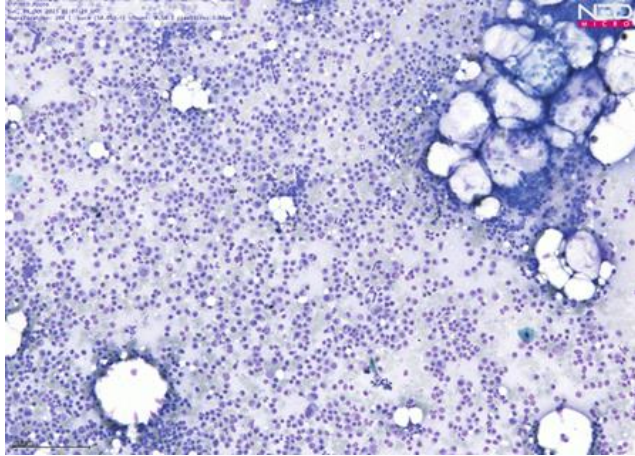
WBC	15,48	$10^9/L$
RBC	3,39	$10^{12}/L$
HGB	124	g/L
HCT	0,356	L/L
MCV	105	fL
MCH	36,6	pg
MCHC	348	g/L
PLT	116	$10^9/L$

NEUT	12,57	$10^9/L$
LYMPH	1,35	$10^9/L$
MONO	0,63	$10^9/L$
EO	0,15	$10^9/L$
BASO	0,00	$10^9/L$
NEUT	81,2	%
LYMPH	8,7	%
MONO	4,1	%
EO	1,0	%
BASO	0,0	%
MIELO	2,0	%
META	2,0	%
PLASM	1,0	%

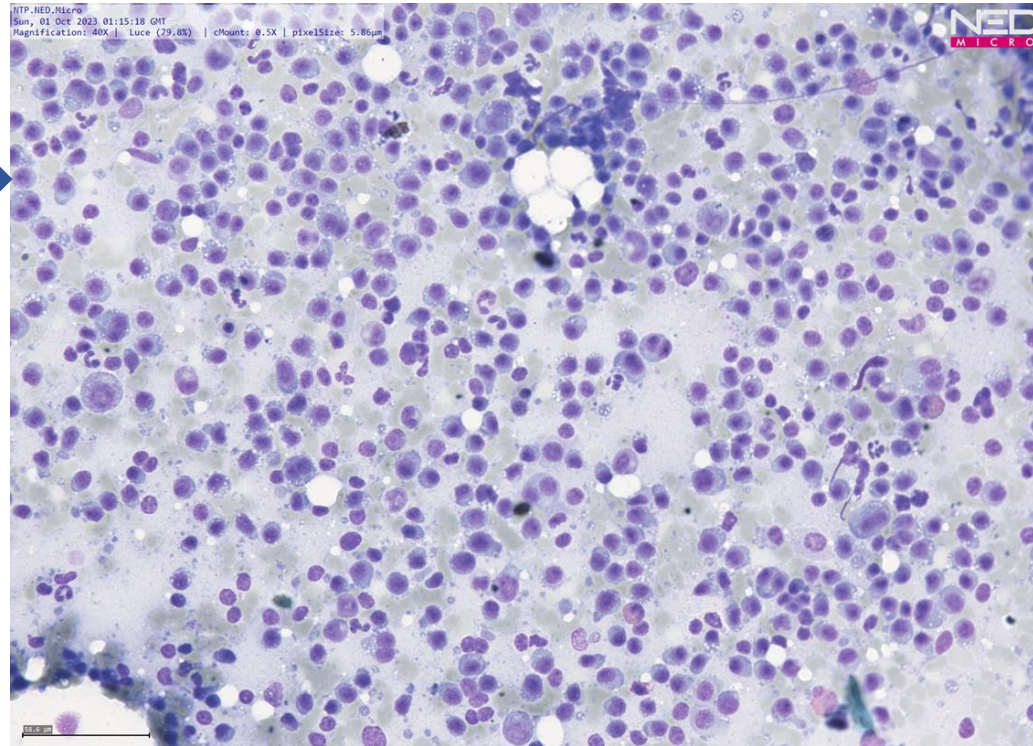
ELETTROFORESI DELLE PROTEINE (S)



CLINICAL CASE

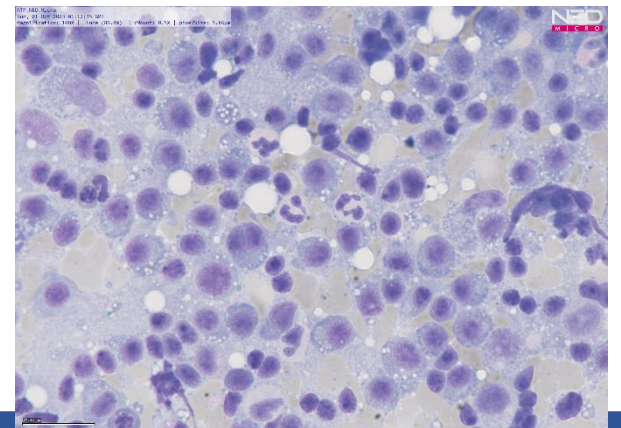
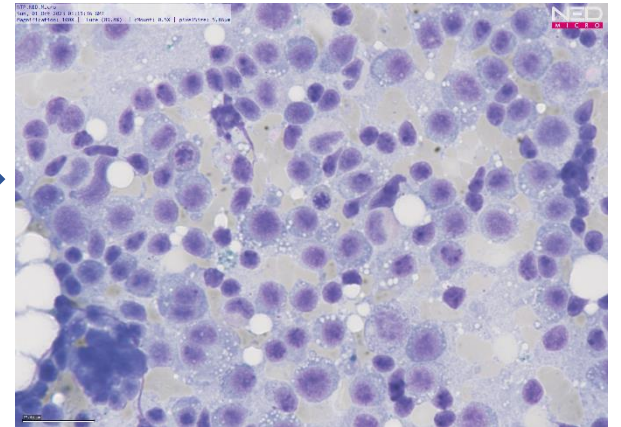
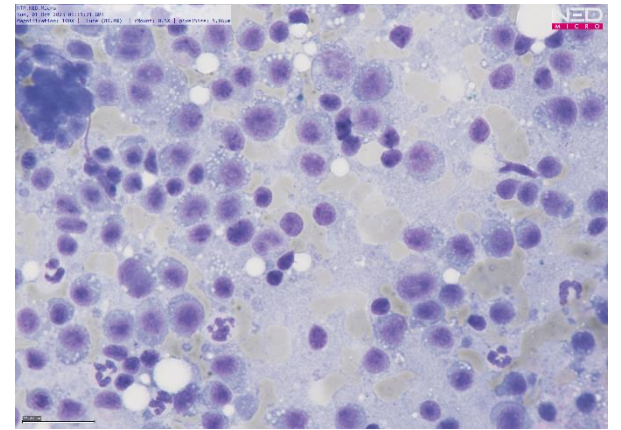


20X



40X

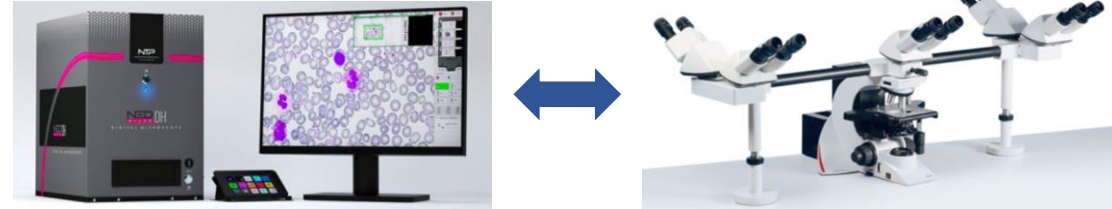
100X



LABORATORY TELEMEDICINE: THE HAEMATOLOGY NETWORK OF THE SOUTHEAST TUSCANY USL

INSTRUMENTAL EVALUATION OF CYTOCENTRIFUGED PREPARATION OF BIOLOGICAL FLUIDS NED-DH VERSUS MANUAL MICROSCOPY

Materials and Methods



- 88 body fluids (48 pleural, 16 BAL, 22 peritoneal, 2 synovial)
- 2 cytocentrifuged slides prepared with May-Grunwald Giemsa panoptic staining
- Cell count and evaluation by 2 experienced operators for reading on NED-DH digital microscope and manual microscope (3rd operator in case of disagreement between the 2 operators)
- The body fluids were analyzed according to CLSI Guidelines (H56-A, C49-A)

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H56-A
Vol. 26 No. 26
Replaces H56-P
Vol. 25 No. 20

Body Fluid Analysis for Cellular Composition; Approved Guideline

Volume 26 Number 26

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C49-A
Vol. 27 No. 14
Replaces C49-P
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Materials and Methods

Statistical analysis:

Passing-Bablok regression analysis and Bland-Altman plot for quantitative comparison of WBC, TC (Total Count of nucleated cells), PMN, MN on manual microscope versus NED-DH and automated flow cytometry count (XN) versus NED-DH microscope.

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H56-A
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Body Fluid Analysis for Cellular Composition; Approved Guideline

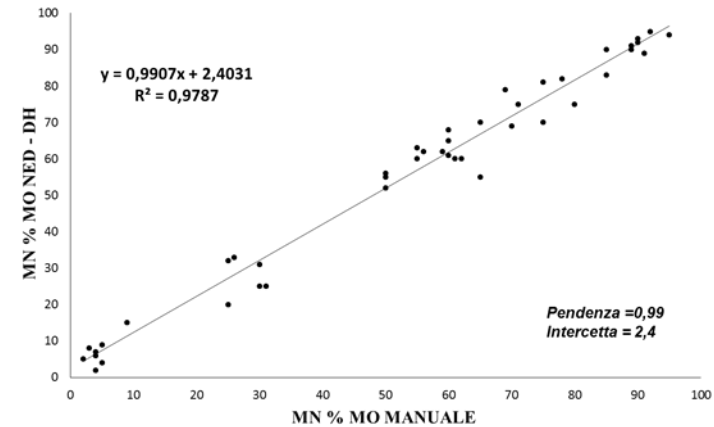
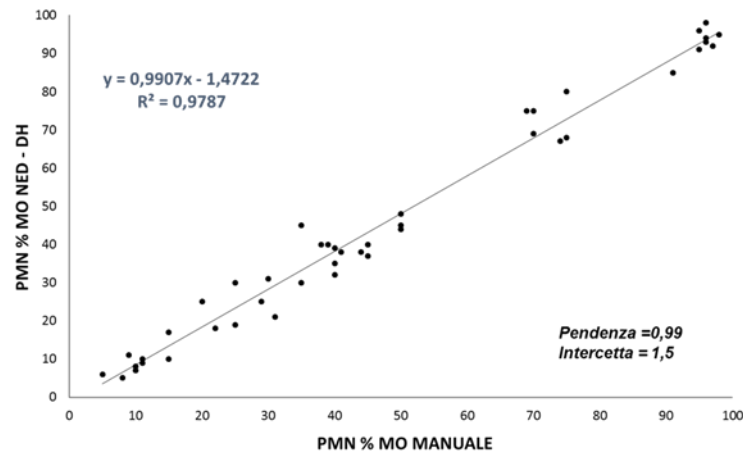
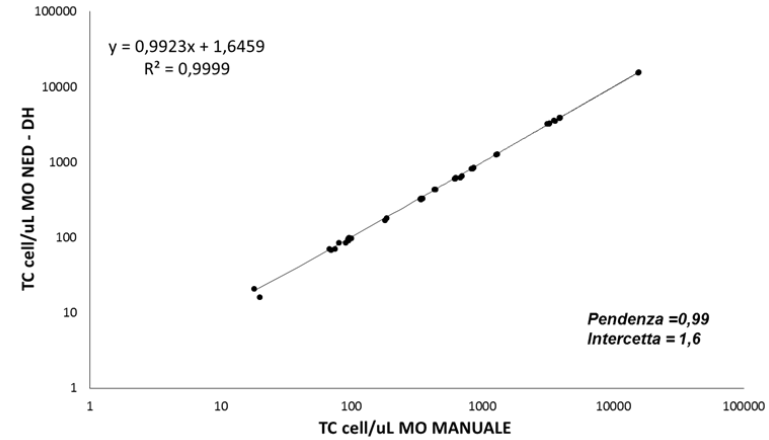
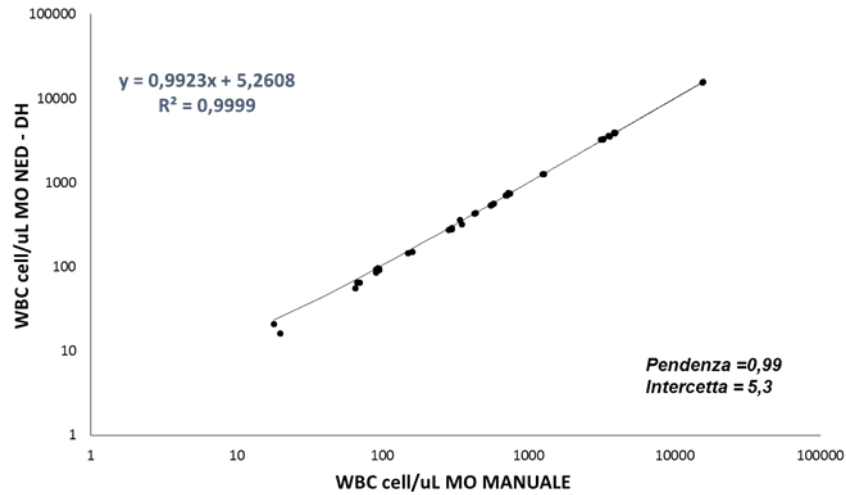
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INSTRUMENTAL EVALUATION OF CYTOCENTRIFUGED PREPARATION OF BIOLOGICAL FLUIDS NED-DH VERSUS MANUAL MICROSCOPY

Passing-Bablok regression analysis

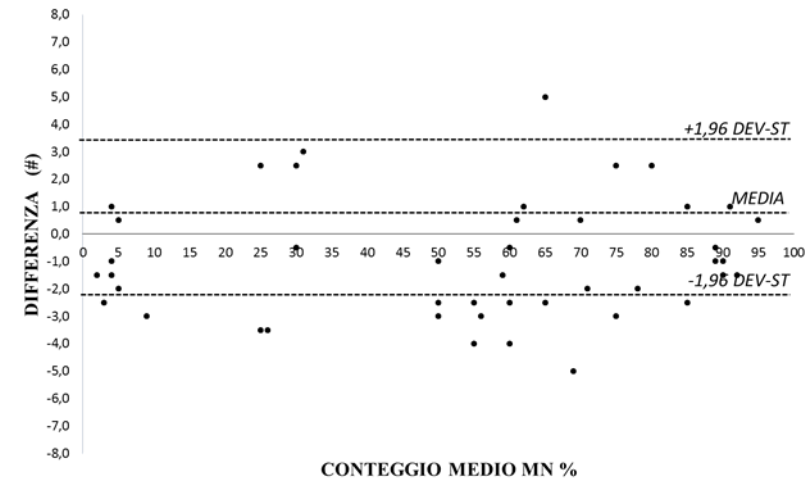
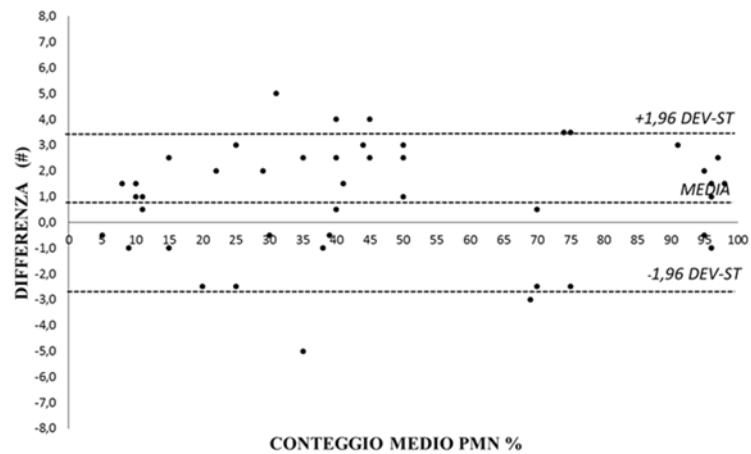
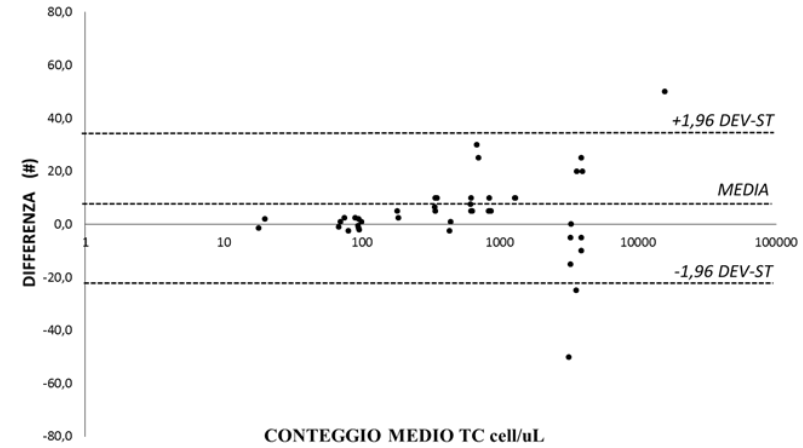
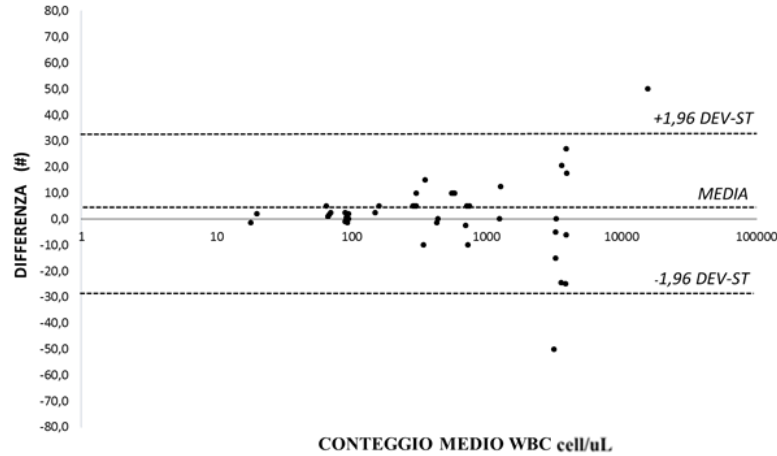
Results



INSTRUMENTAL EVALUATION OF CYTOCENTRIFUGED PREPARATION OF BIOLOGICAL FLUIDS NED-DH VERSUS MANUAL MICROSCOPY

Bland-Altman plot

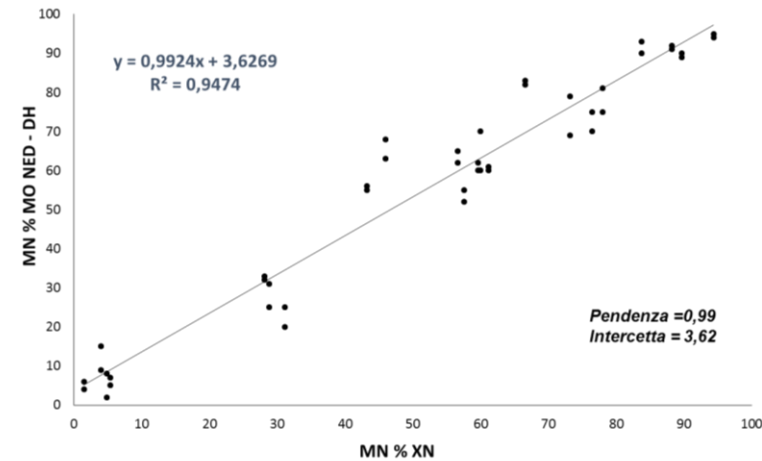
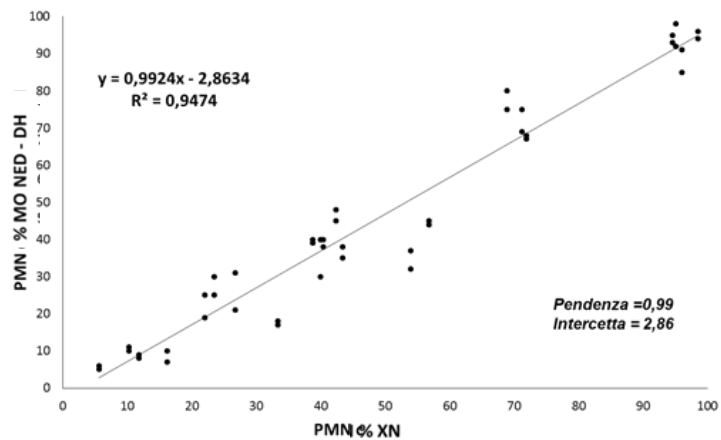
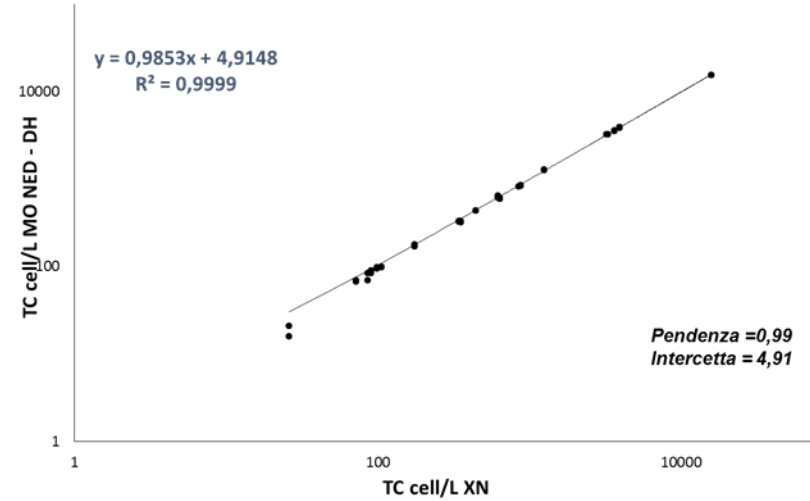
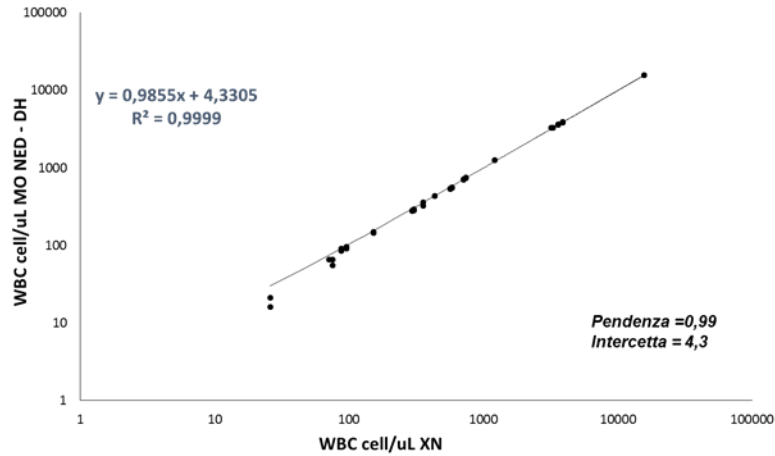
Results



INSTRUMENTAL EVALUATION OF CYTOCENTRIFUGED PREPARATION OF BIOLOGICAL FLUIDS NED-DH VERSUS MANUAL MICROSCOPY

Passing-Bablok regression analysis

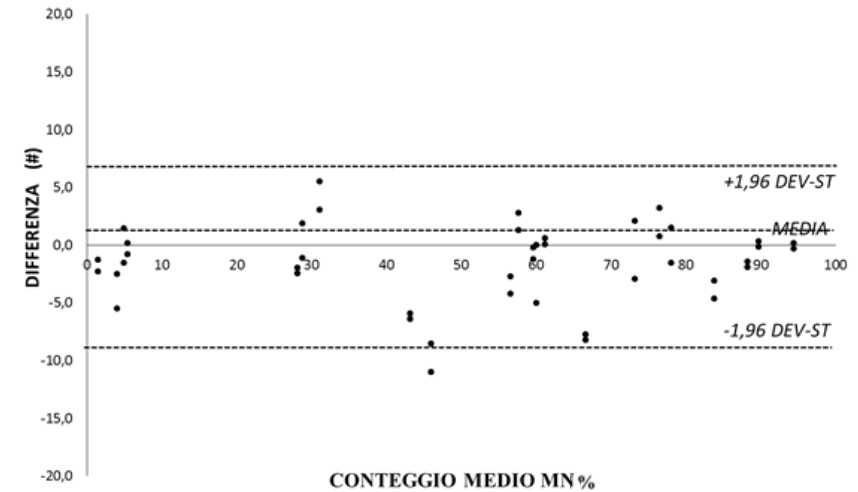
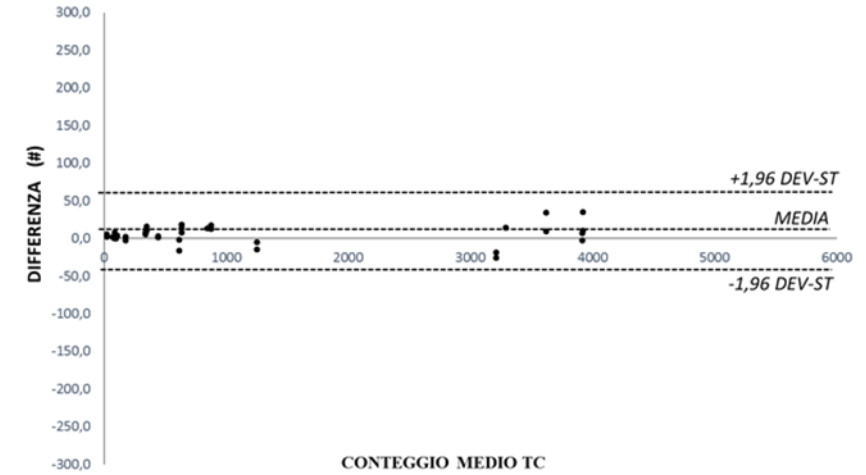
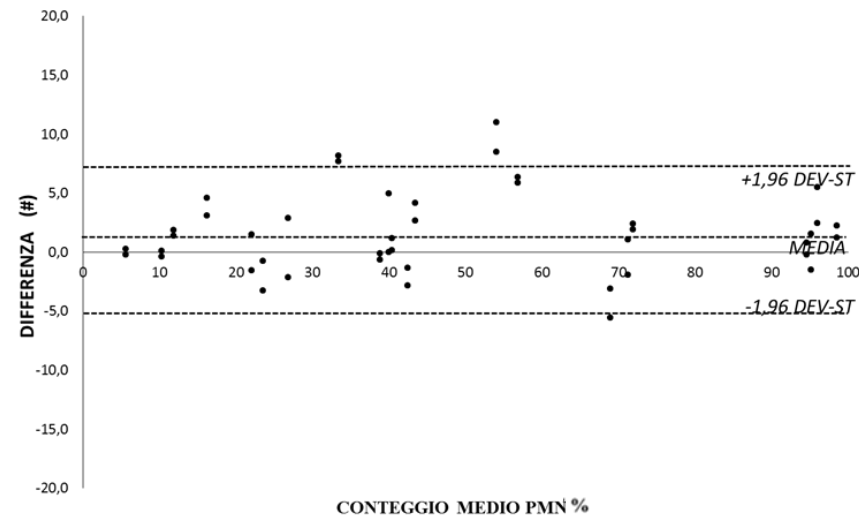
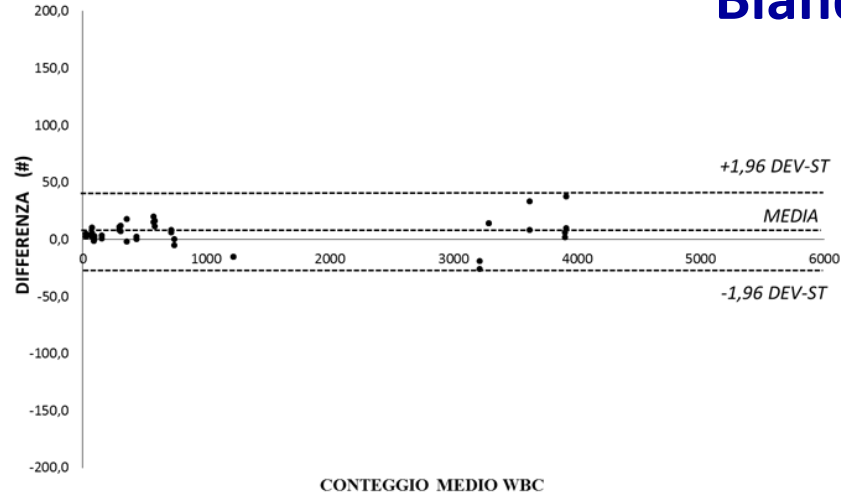
Results



INSTRUMENTAL EVALUATION OF CYTOCENTRIFUGED PREPARATION OF BIOLOGICAL FLUIDS NED-DH VERSUS MANUAL MICROSCOPY

Results

Bland-Altman plot



CLINICAL CASE

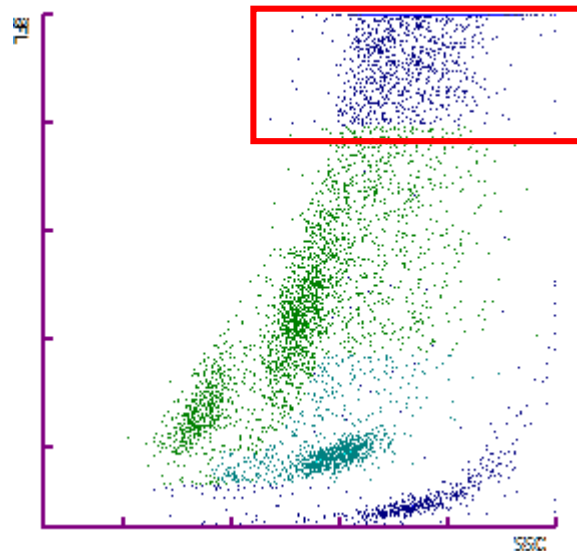
Pleural fluid

58-year-old patient admitted to the pneumology department

Automated cell count by flow cytometry

WBC 356 cell/uL
 RBC 200 cell/uL
 MN 237 cell/uL
 PMN 119 cell/uL
 MN 66,6 %
 PMN 33,4 %

TC 617 cell/uL
 HF 261 cell/uL



Blood Clinical Chemistry Tests

PCR 10,0 mg/dL
 Procalcit. 0,08 ug/L

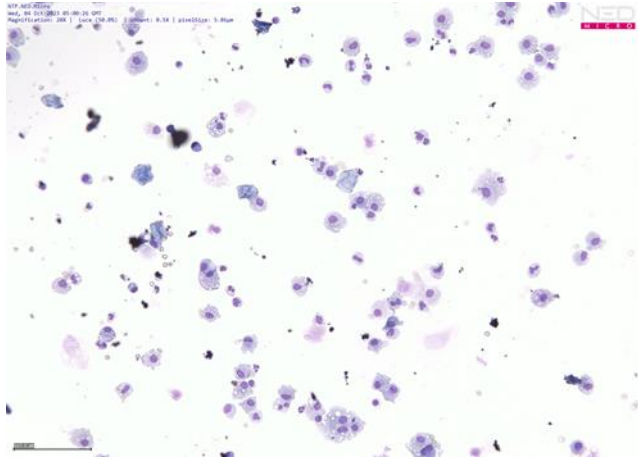
Clinical Chemistry Tests on Pleural Fluid

Glucose 81 mg/dL
 Prot. Total 4,4 g/dL
 Amylase 46 UI/L
 LDH 150 UI/L

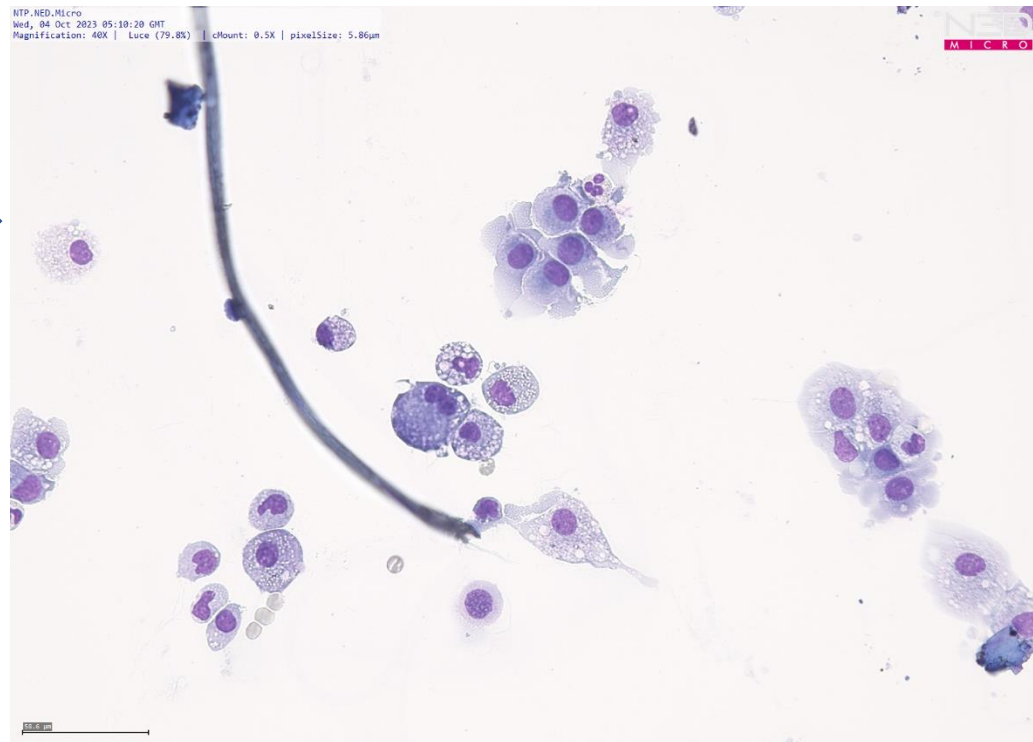
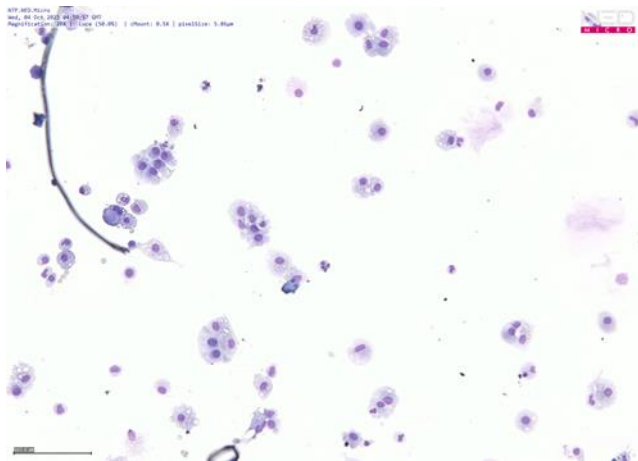
Microbiology Tests on Pleural Fluid

Culture test: *Staphylococcus warneri*

CLINICAL CASE

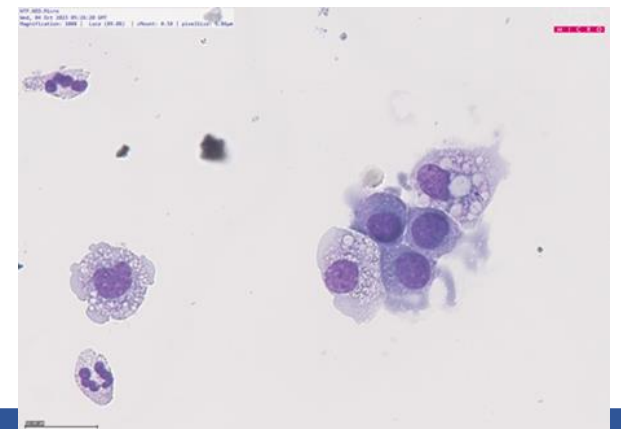
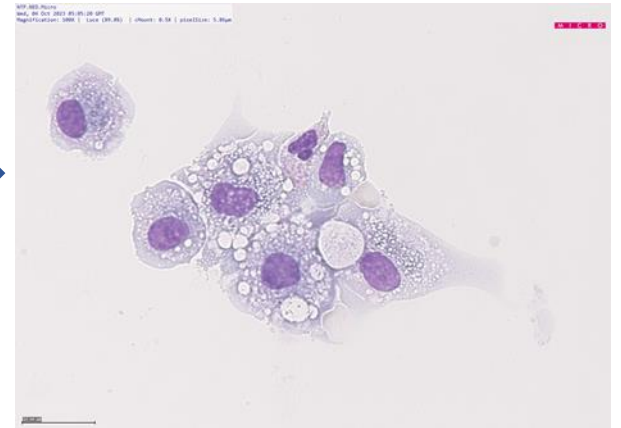
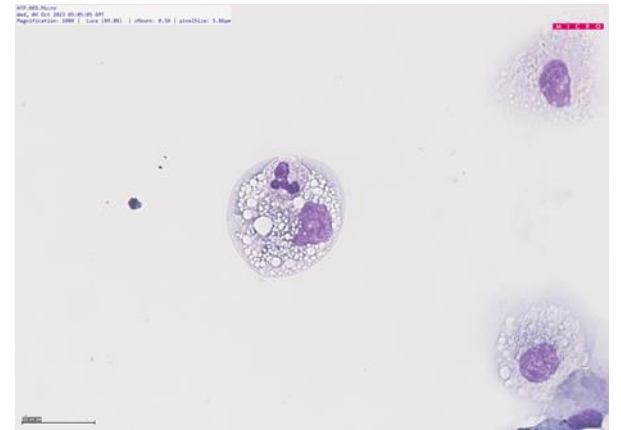


20X



40X

100X



CONCLUSIONS

- Digital Morphology through Tele-hematology and the creation of an analytical network enables management of a challenging and large region like the Southeast Tuscany USL , connecting 12 laboratories through the sharing of data, charts, and cellular images.
- Improved analytical quality.
- A telemedicine network is feasible if supported by advanced IT infrastructure, equipment, and innovative, cutting-edge software.
- Availability of trained and skilled personnel.
- The initial investment is offset by numerous benefits, especially if the network also includes Clinical Hematology, through the sharing of cellular images, placing the patient at the center of a coordinated multidisciplinary team that supports them in all stages of care: diagnosis, therapy, and follow-up.





**THANK YOU FOR YOUR
ATTENTION**

