

Fifteen years of melanomatous meetings

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Background

In 2019, as well as being my last year of service in the hospital, I thought that it would also be the last as the organizer of melanocyte meetings. So, I thought of organizing these meetings as traveling sessions. In February and in March we were hosted in Modena by Anna Maria Cesinaro, in April and May in Reggio Emilia by Simonetta Piana, then in Trento by Mattia Barbareschi. The last-ditch effort was in October and November at the Dermo Clinic in Milan and the grand finale took place in December in Vicenza.

“I am not going back,” I told myself, “I can’t keep managing the whole organization like before.” But in December 2019 I started to regret my decision. When Raffaele Giannotti proposed me to organize our periodical histopathological collegial meetings in the Clinic of Dermatology in Milan, I thought we finally had found a definitive location and solution for the limited capacity house all colleagues in our room in Vicenza. The Professional Education Update Office of the Milan Polyclinic gave us the green light to organize the 2020 edition.

I’d promised myself to be a couch potato, a trout fisherman, a watchful grandfather. Still, the idea of reorganizing the meetings in Milan, in that splendid classroom and having Raffaele and Cesare Massone joining me in a new adventure was fascinating. That damn Milanese “tricked” me once again. He gave me one condition: “Cesare and I help you discuss the cases, since it has become the big monthly festival of Italian melanoma”.

After two meetings in Milan, COVID emergency imposed us to shift them to online webinars, with all doubts and concerns about the results of the incoming meetings. All slides were definitely digitalized by virtual microscope and the virtual meetings were joined also by colleagues from far away (*i.e.* Sicily, Sardinia, Calabria) that had never had the possibility to participate to the face to face meetings in Vicenza or Milan, allowing almost 100 surgical pathologists from all Italy attending the meetings.

Making a long history short, it was a great success.

At this point, the Association of Hospital Italian Dermatologist (ADOI), with Francesco Cusano President and Luigi Naldi Editor in Chief of Dermatology Reports, represented both at the meetings by Cesare Massone, decided to sustain our project.

Therefore, since September 2021 our meetings run on the website and platform of ADOI, where also all the cases are stored in an archive becoming available for ever to all subscribers and best cases will be published on Dermatology Reports.

We were all shocked by the sudden death of Raffaele,¹ that unfortunately never saw the new on-line version of the project. Raffaele was an excellent moderator of the meetings, with his knowledge of dermatopathology, his insight and criticism, and he was always a great support in helping myself and Cesare in organizing the meetings. If today our project has a new life and a green future, we have to thank Raffaele forever.

Once upon a time ...

In 2005, due to mere contingency, I was appointed RAQ (Responsible for Quality Assurance) of the Quality System for Pathological Anatomy of Vicenza. An absurd number of tasks and obligations fell on me, including the necessity to implement a quality control procedure for all the diagnostic reports. I began in my area of expertise, dermatopathology, and started working on the melanoma diagnosis.

I immediately organized a checklist starting from the diagnostic protocols of the CAP, Australian, Canadian and Royal College of Pathologists,²⁻⁵ and I included them in the daily diagnostic routine. The English-speaking countries moved as a Roman phalanx with unparalleled foresight, so I followed their example without delay and organized everything according to their protocols.

Reviewing and sharing with colleagues in the department all the first diagnoses of melanoma, according to the CAP protocols, and trying to equalize them was a problem to solve. With whom should I do this cross-check of all the diagnoses of melanoma made in Vicenza if not with the same people I should be examining? There was no way out; I had to seek help outside my home.

I was not aware of other pathological anatomy centers that had undertaken this path, so I decided without delay to propose it to two well-known passionate dermato-pathologist friends: Angelo Cassisa, who worked in Mantua and Marina Zannoni in Verona. We agreed to monthly meet in Vicenza to review all the melanoma diagnoses made the previous month in three hospitals. So, we started a process that had never been done so systematically in other hospitals. After a few months, I was getting frustrated because the level of concordance of the diagnoses was indecently high. Were we just too good? Or did we like to “play it safe” considering that the lesions reviewed were almost always obvious melanomas?

It was time to raise the bar and extend the review also to the diagnosis of uncertain and complex lesions. In short, we had to think big and do a job outside the protocol. The number of cases to be reviewed was considerable; in case of disagreement, there were no referees, and we did not know what level of K to target for specific diagnoses. We were discouraged, none of us was (or believed to be) a super expert compared to the other two, and we had no idea how to evaluate the deviations.

In these meetings, however, we all discovered that too often, we disagreed on cases that everyone thought were quite straightforward. There were only a few studies reported on diagnostic concordance and regarding only certain types of melanocytic lesions. They were studies organized by large centers of reference where the “players” were almost always the most prominent dermatopathology experts worldwide. They were often depressing studies in terms of level of disagreement that existed even among these luminaries. In an operational context where a general surgical pathologist reads a dermatopathological slide, no benchmark-setting was attempted for defining an expected gap (the delta).

What about the rest of the world?

How the US CAP had elaborated the benchmarks and how the surveys were carried out among the hundreds of accredited laboratories to guarantee an organizational and operational uniformity of the health structures in the country, struck me. The expected ranges on the maximum execution time of an intraoperative examination or the percentage of biopsy samples lost during the pre-analytical processing cycle were no longer a taboo to be silenced; they had been investigated and fixed. The laboratories had to operate below the indicated thresholds.

The motor vehicle industry and other high technological businesses, have already adopted for a very long time a rigorous approach assessing critical issues in their organization management, obsessively aiming to pursue excellence in production processes.

The Japanese cars and motor-cyclists companies conquered the world markets because they were organized with the Lean Six Sigma.⁶ For Toyota, it was a guarantee to produce and fit components of their cars with six precision standard deviations. That equals to no more than 3.4 defects per million items produced with an accuracy of 99.99966%. For all these reasons, I was wondering if it was possible to compare the quality of a car component, or a rocket booster, with the layout of a histological slide. Maybe the layout could be compared, but not the histological diagnosis.

Then, I decided to compare the opinions and diagnoses of a much larger and heterogeneous group of dermato-lover general pathologists to assess the level of diagnostic deviation. Not a Lean Six Sigma, but the study of the modal distribution of the diagnoses for each case.

So, we started this series of meetings in Vicenza. The group grew rapidly in number, and of course, the organization got complicated. We also began sharing cases for a “second opinion” in the classroom, but it was impossible to ask 20-30 personal opinions before the meeting. The “second opinion” was then limited to observation in the classroom using a multi-head microscope. In 2014 everything changed when we equipped ourselves with a slide scanner that allowed us to overcome this limit. Whoever wanted to share a case for a “second opinion,” would send me a section that I would scan and share via Dropbox anonymously with the course participants. The opinion was then sent by everyone, via e-mail to the applicant. The original slide was then revised collegially at the microscope in the classroom for a second check-up.

A first examination read on digital images and a subsequent examination at a microscope: two diagnoses collected in different and complementary locations and observation environments. In this way, we began to collect and share increasingly numerous case studies with substantial shades and different degrees of interpretative complexity. In the past fifteen years, we have collected, viewed, and discussed around 3,000 melanocytic lesions.

Full throttle

Were we willing to get into the arena? Could we do it without defenses and without fear of being embarrassed by bringing complex or wrong diagnoses into the classroom? We, the first three explorers, had established a gentlemen’s agreement that we never betrayed or changed since that day.

Fourteen years later, the group of the “three daredevils” has grown to the point that we had a mailing list with a hundred pathologists and dermato-pathologists of different professional backgrounds with whom we’ve shared digitized cases that we’ve then studied under the microscope in the classroom.

A hopeless challenge?

Over the years, we understood how spitzoid lesions were very conflictual and complex. Remember the nightmare of Lorenzo Cerroni’s 2008 tutorial in Graz?⁷ In very complex cases, the ten best dermato-pathologists in the world had extremely low diagnostic reproducibility and agreement. For us, reproducibility was a damn big problem even for superficial, regressive, and sclerosing lesions, or for lesions that “pagetised” very little; in short, the melanocyte universe included them all a bit. The time had come to praise the uncertainty and the ability to diagnose it without fear of unpopularity. My uncertainty was often not the same as the others and vice versa. There was no habit of comparing and sharing cases. On the same observation, the mental path and value attributed to microscopic parameters were often different between several pathologists.

I had a vision

What makes melanocytic lesions and the microscopic examination such a special and varied medical act, that may be sometimes trivial, sometimes complicated, and potentially full of pitfalls?

I started to wonder why some colleagues have an out of ordinary talent at the microscope, and, despite devoting so much time to studies and microscopic observation, others remain in the limbo of just an average skill? Why, moreover, are some excellent in distinct areas of pathology and modest in the melanocytic field?

The world “within”

There is a world that I call “within” that resides in our minds of morphologists, that manages a special skill, which is crucial to possess and improve from the early stages of our professional growth. If our parents provided us with this special neural network, we would become very fine diagnosticians in a short time; otherwise, we must look for alternative ways with specific training to become one.

It is not a conscious skill, but it is there, sitting next to us at the microscope. It can guide us correctly through the process of drafting the diagnosis and make us unlikely to miss a trivial diagnosis.

It is a form of cognitive intelligence that has been codified by the theories of Gestalt psychology,^{8,9} and that feeds on shared contents (swarm intelligence).^{10,11} Soon probably these theorems may be the substratum to elaborate techniques to train professionals to the vision and diagnosis under a microscope.

Perception according to Gestalt

The Gestalt psychology or psychology of form has theorized that all the perceived in its wholeness is the fusion of details rather than the arithmetic sum of the individual details;^{8,9} it is not necessary to count melanocytes or keratinocytes to diagnose nevus or seborrheic keratosis. Just look and let the individual units of the slide image be processed and merged to obtain the final shape in our world “within” that is transformed by our neural network into a definitive diagnosis. In fact, the motto of the Gestaltists was, “The whole is more than the sum of the individual parts.” With a glance, we always have a first perception and a ready diagnosis (belly gut feeling diagnosis), then the brain works on adding or subtracting patterns of the image in a functional way, according to

precise rules, the laws of Gestalt.

The laws of perception formulated by Gestalt decide the fate of our life as pathologists. In our eyes, an image can be meaningless, like written words to the mind of a person with dyslexia, who can more easily recognize only letters. All pathologists recognize individual images and colors, but not everyone can see the overall figure evoked by the perceptive addition of the individual images and colors, which then has a diagnostic significance.

Think of Arcimboldo, a Milanese painter (Figure 1) and portraitist, who in the 1500s used a compositional technique of faces in his paintings that only four centuries later would have been identified as fundamental by Gestalt vision psychologists. He used fruits and vegetables to build and characterize faces. It is a pity that poor Arcimboldo was labeled as a lewd, ridiculous painter.

I began to read the works of Gaetano Kanizsa, founding psychologist and Director of the Institute of Psychology of Trieste and of Paolo Bozzi one of his most famous assistants and most brilliant experimental phenomenologist. Kanizsa, artist and psychologist of Gestalt extraction, has written numerous papers on perception, and on the mechanisms of figure-background articulation.¹²

Paolo Bozzi,¹³⁻¹⁵ philosopher and eclectic scientist, for some years taught at the universities of Padua and Trento, before taking up the chair of Methodology of the Behavioural Sciences at Trieste. He was one of the most subtle thinkers among Italian experimental psychologists and founder of what later came to be known as “naïve physics”.¹⁴ According to him, experimental phenomenology was conceived as the method to combine laboratory experiments and observations of everyday life.

To quote him:¹⁶ “What I’m emphasizing is that our knowledge covers only about 10% of the properties present in the world that surrounds us and that the remaining 90% has still to be discovered. If we do not seek, we shall not find. These are the kind of facts that physiology will have to explain, and not a simplified perceptual world that simply does not exist. This more complex world is what has to be explained by informatics or by the different branches of the neurological sciences, because this is the real world of vision, not that impoverished and approximate world that we carry in our heads as our image of visual reality”.

The new working-group

No mentor in the laboratory has ever explained to us how to extract significant diagnostic patterns from slides, how to mentally segment the visual field, or how to scotomize particular objects, perceive them above or below another, and how to name a figure as a whole.

Fascinated by Gestalt theories, I searched for other proselytes to expand the group. Roberto Ricci (Parma), Gerardo Ferrara (Benevento), Anna Maria Cesinero (Modena), Elizabeth Picciotti (Naples), then again, more and more people have joined the group. All united by the same desire: to discuss, be together and learn from others under the microscope.

So, we decided to create a study group that was open to anyone interested in sharing and discussing case studies. To make the course more attractive, I decided to credit it with ECM (Figure 2).

It seemed that we had really done it and that everything could go smoothly and without any hitches. Three critical issues emerged.

First problem: the level of experience

Among the participants, we immediately noticed a discrepancy between expert pathologists, pathologists with medium experience, and beginners. I decided, although not without some difficul-

ties, not to divide the groups, and I did everything to harmonize the components and understand the need to prioritize the transfer of experience between people.

Second problem: the individual value of the experts

Another problem emerged during the meetings: the weight of the opinion of the experts compared with the total number of participants. If a lesion was considered to be malignant by 20 young observers and benign by 5 experts, what was the correct attitude to keep for the assessment of the final judgment?

It was evident that the weight of competence was a real problem if it was being underestimated compared to the number of participants. A dominant expert opinion, on the other hand, would have overshadowed the “less expert” evaluation, albeit significant for the study of the modal distribution. It means that in not super specialized contexts, the “less experienced” diagnosis would have been the most probable diagnostic conclusion, the one everyone would pin out in a challenging case.

I presented the problem to Edi DeFrancesco, an economist at the University of Padua who advised me, to solve the competence problem, by introducing an individual evaluation parameter of the participants indicative of the diagnostic authority of each one of them. The final result of the diagnosis, therefore, would have taken into account coefficients characterizing the diagnostic experience (ability). In this way we could avoid the assessment of 10 benign lesions against 10 malignant lesions without knowing in which group the most experienced were. The conflicting judgment of the two groups was compensated by the “coefficient of competence” rather than a mere numerical representation of the diagnoses.

The proposal created discontent, a great embarrassment among the participants. It was considered discriminatory and was later rejected by almost all, for ethical reasons. My explanation attempts and reasoning, in the face of obstinate and embarrassed refusal, were of no use. No one wanted to “weigh” the diagnostic competence and reputation.

In any case, we identified an indirect parameter of diagnostic complexity and interpretative conflict of the parameters observed in specific diagnostic contexts.

Third problem: the language

It soon became evident that interpretative tones were often not easily translated into spoken language due to the lack of an adequate vocabulary. The ability to define precisely a shade of color or shape was not so important, as to communicate in a comprehensible way the perception of those diagnostic aspects evoked during the observation.¹⁷ People often do not have linguistic labels for abstract concepts and get stuck during the oral statement. Even the most experienced, cornered by questions, often lost patience by puffing an “I don’t know, but for me, that’s the way it is.” Qualia of lesions (short for qualities of visual objects) have primary quantitative properties (area, thickness, cellular density, shape, patterns) and secondary and tertiary qualitative properties which are exquisitely subjective aspects of personal experience and consciousness.

Such subjective properties belong coherently to visual awareness. The lack of linguistic labels and of a common and coherent visual grammar may explain how is frequently very difficult to state exactly how two similar lesions differ, even though a difference is clearly perceived.

“Opsieme” is the explanation to everything

Jean Paul Curchia,¹⁸ vision scientist of the department of ophthalmology of Marseilles elaborated the concept of “opsieme” or

unity of vision, as the smallest significant visual unit.

The shapes, the colors, the orientation of the elements that create the image, are seen with maximum sharpness at the fovea and with blurred limits in the surrounding retinal areas. This entails the need to move the eyes quickly (and hungrily) to capture clearly the perifoveal particulars. The image must be acquired in order to have a significant identification, and the speed of this process can be very different from person to person. For some, it may be necessary to be at the head of the slide to feel confident in the rapid and complete observation of these significant points.

Just like the letters that form words need to be recognized to evoke a phonological awareness (*grafeme*), so the images, according to Curchia, must be segmented and mentally reassembled to be paired with their own mental maps and be recognized as diagnosable entities. Like in grammar, words must be placed in a suitably natural way to express precise concepts, so “*opsieme*” must be well perceived to ensure a meaningful vision and may differ numerically and topographically between individuals.

As such, the fundamental visual element or elements must be perceived, extracted, and presented as meaningful units to the mind so that they may find a matching diagnostic map to make each of us consider possible a specific diagnosis. Those who have a diagnostic doubt did not perceive the minimum visual elements complementary to their diagnostic map. Just as each context has a basic identifying unit (phoneme for a word, grapheme for a significant phrase), the “*opsieme*” is identified as the smallest significant visual unit. A sort of elementary visual equation capable of indelibly linking the components of the image to clinically significant entity. Consequently, the diagnostic points on which to base the construction of a diagnosis or a diagnostic pattern, can be unique, a few or many, rapidly acquirable or vague and slowly acquired for others, or even absolutely invisible to some.

The role of the digital scanner

The scanner made it possible to digitalize histological slides and represented a formidable tool for digital observation training.

The cases proposed for discussion and scheduled for the next meeting, came to me already digitalized or with just a slide that I scanned at that moment. The digital images, distributed to the participants of the study group, were studied at home first, and the slides were subsequently observed in the classroom under a microscope, possibly also with additional immunostains.

The diagnoses made first in telepathology and then under the microscope, were coded, collected in a database and processed in a post-meeting report that summarizes in graphical format the outcome of the discussion for each case.

The modal distribution of the diagnoses formulated in the two observation environments was evaluated. The histograms showed their grouping in three main diagnostic classes (benign, doubtful, malignant) with an indication of the number of observers. Some parameters of subjective judgment of the digital case were also evaluated (interpretative complexity, need for special coloring or additional diagnostic techniques, and the degree of diagnostic confidence). In case of a spitzoid lesion, the risk class is evaluated according to the aggregate criteria by Urso (Figure 3).

Afterthoughts

Each diagnosis consists of a series of complex neurophysiological and mental processing events, which, within a few millise-

conds, from sequential retinal images transmitted to the visual cortex, leads to diagnosis with the intervention of other complex, very rapid memory and cortical activities of elaboration.

In contrast to the traditional Gestaltic and “modular” understanding of perception, according to which visual processing is encapsulated cognitively and (im)penetrable from higher-level processes, a tidal wave of recent research alleges that emotional states (beliefs, desires, motivations, intentions, and linguistic representations) exert direct top-down influences on what we see.¹⁹ In this way

Today I am amazed at how we have been able to build such an experience with patience and grow a diagnostic skill without ever having carried out targeted training on these perceptive mechanisms. The talent or the difficulties encountered by some in the diagnostics clearly indicate the existence of an innate predisposition or a specific difficulty in the recognition and mental elaboration of some significant forms, as happens in other areas for learning disabilities (dyscalculia, dysgraphia, dyslexia).

The diligent study, the freedom of access to diagnostic material, the possibility of exchanging information, and the parameterization of the morphological aspects is what we need to improve and train continuously but there is an enormous space of intervention useful to improve these skills.

Time has come to try to insert specific training programs with the intervention of technical figures specialized in the study of the mechanisms of vision. An impressive literature corpus does exist, and outstanding vision scientists devoted to the field of Experimental Phenomenology could open a new era to our professional learning and teaching courses.²⁰ If our job was a high paying sport the available funds would have allowed us to follow specific training, and we would be “light years” ahead in the diagnostic ability at the microscope.

Melanocytic lesions are not only a chapter of dermatopathology; they are a world that needs a profound knowledge of microscopic anatomy, physiology, genetics, and clinical information for a formally correct approach to their study.

But all this is not enough, because the rest is talent and those who are not born with it, however, can increase it by training their perceptive skills and the ability to modify mental maps with study and continuous training made of discussion and comparison.

Dear Reader, I urge you to think that the future will be characterized by the presence of droids that we are already training today with the idea of making them better than us. Are we really aware of the danger that could represent to our professional survival if we do not introduce new teaching paths? Today the morphological parameters we use for diagnostics begin to be translated into machine language based on algorithms free from higher-level cognition effects.²¹

Will our head alone and a microscope be sufficient to guarantee our survival in a world where our possibility of error could be statistically too high compared to that of a machine? Will the droids join us like in Star Wars on the spaceships *en route* to some distant galaxy to help us and suggest the best diagnosis, or will they do everything to disempower us?

This Flash Gordon ending makes us smile, but I assure you, as a big fan of science fiction, I can't help thinking about it (and worry about it).

Today I still spend my time discussing under a microscope to expand my mind maps. Between us and robots, in the long distance, we will win again, but young people will have to be much better than we are now because the competition will be ruthless (Figure 4).

I'll be fishing for trout. You can bet on it!

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Figure 1. Left: Arcimboldo self portrait, Národní Prague Gallery. Right: Autumn, 1573. Oil on canvas, 76x64 cm Musée du Louvre, Paris.

Discussione di casi clinici e analisi dell'attività in diagnostica del melanoma e delle lesioni pigmentate atipiche (Cod. ECM: 1777-252163)
 • casi presentati: 22 (11 QC; 11 2nd opinion)

Tipo	Quadrante	Case n.	Patologia		Prima		Seconda		Terza		Patologia		K. Ricca	
			Mc	Digital	Mc	Digital	Mc	Digital	Mc	Digital	Mc	Digital		
QC	✓	Sarofino	19-2151	7	7	7	7	7	7	7	7	7	7	7
QC	✓	Aringano	19-4216	36	36	16	36	36	36	36	36	36	36	36
QC	✓	Lipalta	19-1288	11	11	11	11	11	11	11	11	11	11	11
QC	✓	Calare	19-4882	5	5	5	5	5	5	5	5	5	5	
QC	✓	Farma	19-21416	12	12	3	7	7	7	7	7	7	7	13
QC	✓	Farma	19-21887	12	12	7	7	11	11	11	11	11	11	11
QC	✓	Sarmone	19-2867	7	7	7	8	10	8	8	7	8	8	8
QC	✓	Vicenza	19-09200	25	25	25	25	25	25	25	25	25	25	25
2nd op	✓	Neoli	19-10385	1	1	1	1	1	1	1	1	1	1	1
2nd op	✓	Genova Surlab	19-16745	8	8	3	8	8	8	8	8	8	8	8
2nd op	✓	Venona	19-16858	6	6	3	6	6	6	6	6	6	6	6
2nd op	✓	Cremona	19-1913	8	8	8	8	8	8	8	8	8	8	8
2nd op	✓	Cremona	19-18709	8	8	8	8	8	8	8	8	8	8	8
2nd op	✓	Imole	19-11474	2	2	1	2	2	2	2	2	2	2	2
QC	✓	Milano (Civico)	19-217	23	23	23	23	23	23	23	23	23	23	23
QC	✓	Roma Sapienza	19-21308	16	16	16	16	16	16	16	16	16	16	16
QC	✓	Roma Sapienza	19-21397	16	16	8	16	8	16	16	16	16	16	16
2nd op	✓	Ragusa Iralia	19-16748	19	19	8	19	19	19	19	19	19	19	19
2nd op	✓	Ragusa Iralia	19-12168	5	5	3	5	5	5	5	5	5	5	
2nd op	✓	Desenzano	19-9842	2	2	1	2	2	2	2	2	2	2	2
2nd op	✓	Tronto	19-19946	8	8	8	8	8	8	8	8	8	8	8
2nd op	✓	Torino	19-6993	22	22	22	22	22	22	22	22	22	22	22

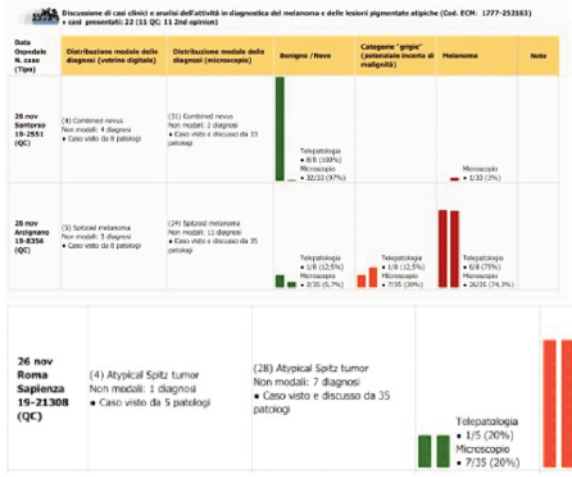


Figure 3. Discussions.



Figure 2. Poster of the event.