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Review

Whole body plastination, intra-organ heterogeneity, and tissue based diagnosis – a survey

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Abstract

Background: The corpse is the final structural relict of life. Its detailed analysis, the autopsy formed the basis and contributed significantly to our understanding of location, function and interaction of organs in man. Today, autopsies are performed rarely. They have been replaced by radiological in vivo visualization techniques and the analysis of organ excisions and biopsies. Which attributes do whole body preservations possess in this context?

Techniques of Whole Body Analysis: In vivo imaging transfers the appearance of body organs and cellular structures in virtual images. The patient's exposure to X-rays, fundamental particles (electrons, positrons, etc.), strong magnetic fields (nuclear resonance), or ultra sounds release the corresponding signals. The obtained images are interpreted in search for local abnormalities such as cancer, acute and chronic infections, inborn errors, hypertrophy or atrophy.

Autopsies require the removal and visual inspection of organs shortly after the victim's death. In addition, tissue probes of suspicious lesions are fixed and microscopically analyzed. The search for gene or protein abnormalities are added dependent upon the clinical history and gross findings.

The whole body plastination is performed in separated steps which include fixation, anatomical dissection, forced polymer impregnation, positioning and curing. Organs and other tissue structures can be taken out of the body and separately demonstrated, or aligned and fixed within the body. Additional tissue examinations are possible at this stage, which is followed by hardening and fixation of the still flexible body. Fixation is done with heat, light or gas.

Results and Interpretation: Tissue conservation is a prerequisite to analyze and investigate in diagnosis and forecast of disease occurrence and behaviour. In history, autopsies have opened the door to localize the position and to understand the functions of organs. Today, they have been replaced by tissue banking and in vivo examinations in a wide range, especially when local

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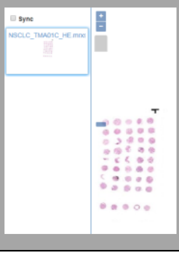
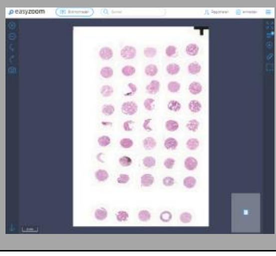
lesions of organs are under investigation. Analysis of blood and serum is the main technique to search for organ dysfunction. Whole body plastination is an appropriate technique to investigate and demonstrate healthy appearance of organs, intra-organ heterogeneity, connection to and communication with neighbouring or distant organs as well as localization and distribution of organ lesions, and the associated functional impact.

Perspectives: Modern societies try to inform their citizens by numerous investigations of the public health status and to improve the health condition as well as to minimize the development of behaviour associated diseases such as smoking and lung cancer, or overweight and infarction. Well performed body conservation supports these efforts. In addition, it can be considered an innovative technique to understand, diagnose, and even treat dysfunction of intra-body communication at the physical and even mental level.

Keywords: Body Worlds, plastination, autopsy, liquid biopsy, in vivo imaging.

Virtual Slides:  

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Introduction

Any living system is characterized by structures and associated functions that are located within a circumscribed well defined body [1, 2]. In principle, structure and function are of the same nature, if associated with the duration of observation [1, 2]. The observation time in medical diagnosis might be long, or short, if compared to that of the compartments of investigation. It is long for blood, serum, protein, etc. analyses. These investigations measure changes which are associated with the disease's intensity. The observation time is short if the existence of a disease should be detected or classified; for example, if the cell type of cancer should be determined by biopsy or surgical exploration [3, 4].

According to ancient documents, knowledge and classification of human diseases probably started with the observation of symptoms, investigations of excreta or traumata, and visible changes of the skin. They allowed to forecast the viability, and to draw some associated conclusions of potential intervention, treatment, and related internal, not directly assessable

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composition of the body [5, 6]. The knowledge of the organs' position inside the body was poor and did not at all correspond to the reality <see figure 1> [5].

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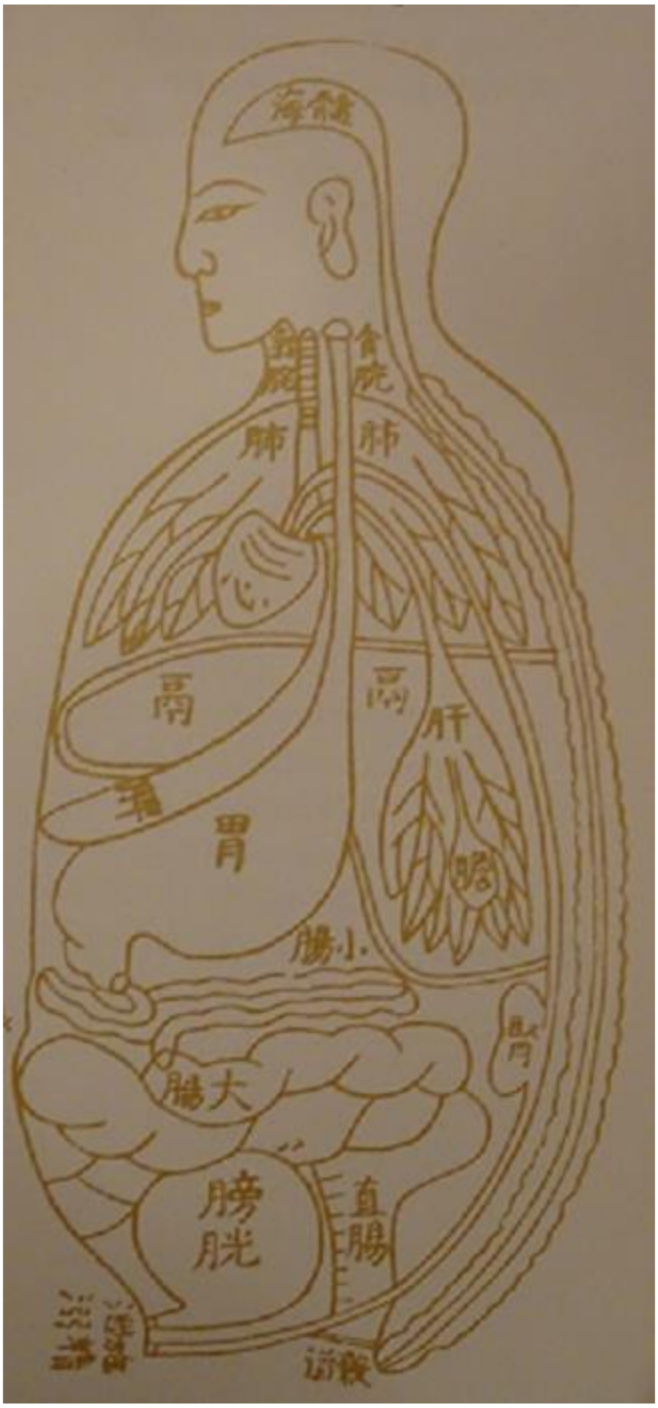

Figure 1: Antique Chinese map of an abdomen (according to Yang Ki-Tscheu) [5].

Ancient Chinese drawings or Greek medical reports demonstrate that not only the structural body composition but also basic mental functions such as visual recognition, hearing, speech, emotion, knowledge, have been completely wrong associated with the responsible body organs

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[5, 6]. For example, the Greek thought that mental functions are located in the knees and not in the brain [6].

At that time the most advanced knowledge of the body was derived from fighting and war. It was well known which body parts were the most vulnerable and exposed to fatal strikes with cut and thrust weapons [5, 6].

Hunters and priests knew probably very well the inside of slain or sacrificed animals. However, they have not been able to transfer their expertise from animals to man [5, 6]. The humans of the stone ages ate organs of killed enemies and might, therefore, knew some anatomy of intern organs; however, most of these habits have probably been performed during religious ceremonies, and, therefore, have not been transferred into natural considerations, i.e. time and space independent observations.

The same statement can be said from the priests and medical doctors of the ancient Egyptians: They performed numerous mummifications, however, did not transfer their knowledge of organ localization and associated functions into detailed anatomy. The mummification itself was performed by assistants and not by priests or medical doctors, which might explain the strange situation [5, 6].

Despite these confirmed historical facts, the performance of autopsies ranges back to the ancient Greeks who again firstly tried to derive reproducible medical knowledge from symptoms and superficial observations, and then changed from a theoretical concept to observation.

The milestone of the development of natural sciences can be awarded to Aristoteles (384-322 BC) who was probably the first anatomist. He performed autopsies by himself and could prove that the heart is the center of the bloodstream and that the kidneys produce urine [7]. Erasistratos (320 BC) intensified these efforts and performed more than 600 autopsies, not only of corpses but, in addition, also of still living condemned criminals [7].

Modern autopsy performance was introduced decades later by Andreas Vesal (1514-1564), Brussels, who asked Stephan von Kalkar, a Tizian Student, to draw a standing corpse with stressed arms which indicate physiological muscle movement [8].

These anatomy analyses matured to modern autopsy performance, which usually starts with an inspection of skin and external abnormalities followed by the opening of the corpse, remove of internal organs and their inspection [9-13]. Fixation of the body and organs is usually missing. Only small biopsies are taken, fixed and investigated under the microscope. Gene and protein analyses are added if needed [4, 14-18].

The morphological observations were documented on paper drawings and used for education and potential explanation of the supposed disease. Italian and Dutch anatomists were the leading medical scientists in the 16th and 17th century. A characteristic autopsy document from that time is shown in <figure 2> [5-7, 19].

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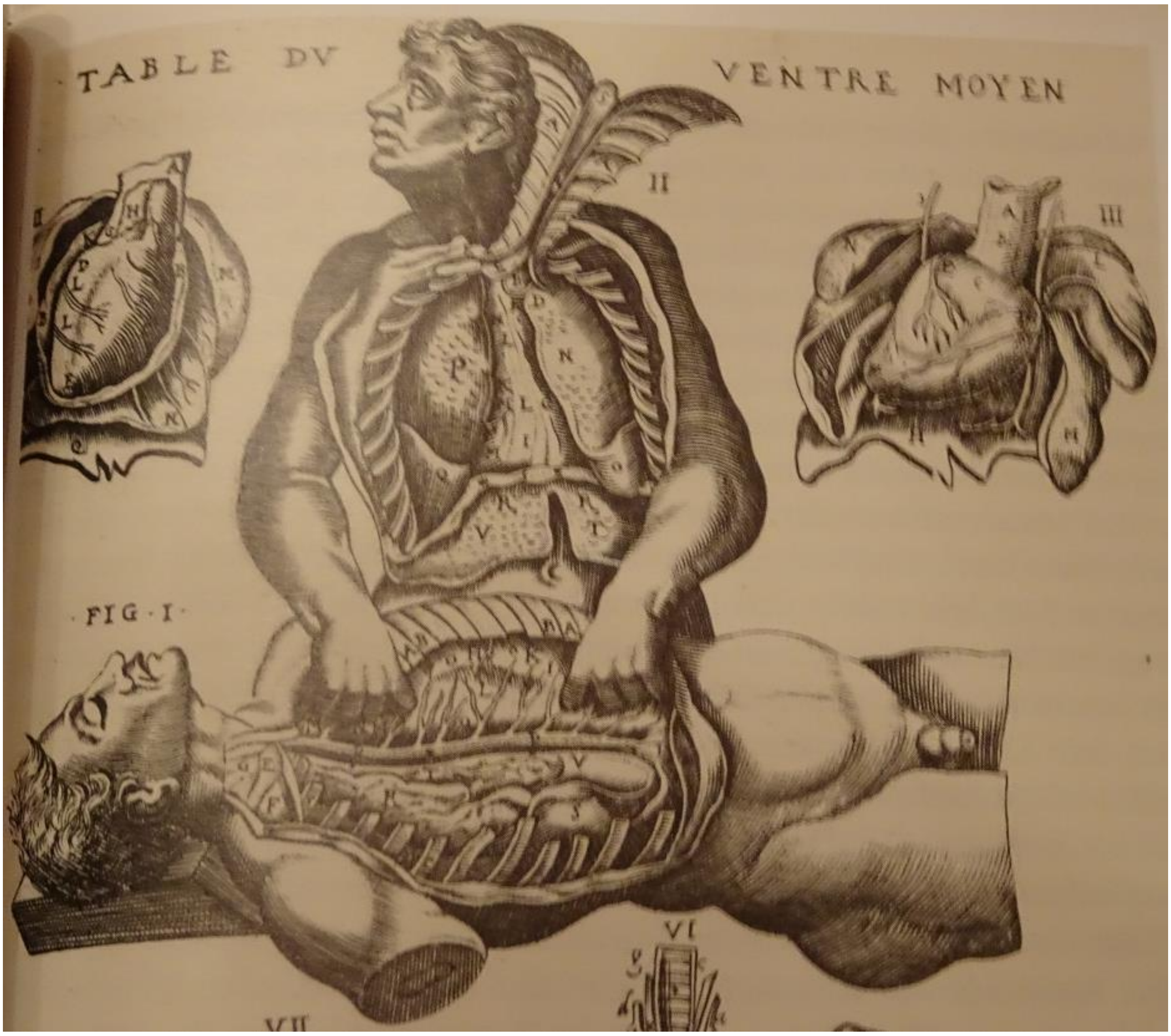

Figure 2: Autopsy performance during the 16th and 17th Century, Italian school.

The principal performance of autopsies is still in practice today. The body is opened, the organs are removed, and investigated without preceding fixation. Conspicuous parts are sampled, fixed, and microscopically, and biochemically etc. analyzed [[20-23]].

Whole body plastination (preservation) has been derived from the autopsy performance in the 1980th [11, 15, 24-28]. It started with organ and whole body cross sections followed by careful preparations of the whole body. It can be compared with the early beginning of autopsies which tried to combine morphology with an idea of body and organ function.

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In contrast to an autopsy, the whole body plastination starts with the preparation of individual organs and following fixation of the body including untouched organs. The following dissection and precise preparation of organs is directed by the idea to demonstrate the activities of those organs that are involved in a predefined function. Examples are muscle movements, which are involved in a jumping goal keeper, head, brain, eyes and arm of a reflecting chess player, or body position of a horse rider. Additional preparations include the skeleton of arthritis persons, smoker's lung, and haemorrhage.

What are the prerequisites to create an accurate and awesome whole body preparation?

Details of whole body preparations

The whole procedure starts with a certificate of the body donor which ensures the permission of the living person to perform a body plastination after her / his death. This certificate is obligatory and can partly be compared with an organ donation [19, 28, 29].

The certificate permits the anatomist to preserve the corpse and to display the morphologic alterations of certain or all body parts in close association with their specific functions, for example muscle tension, thinking, trauma, etc. [1, 5, 6, 8, 17, 19, 26, 27, 30, 31].

The final aim of a plastinate is reached by four steps which include 1) fixation, 2) dehydration, 3) impregnation, and 4) hardening [11, 25, 32].

Fixation stops the otherwise unavoidable decay of tissue. The principle fixation techniques include deep freezing and the installation of fixation fluids such as formaldehyde, acetic acid, alcohol, or HOPE [33, 34]. Formaldehyde fixes the tissue fast. It is the common fixative in surgical pathology. Its disadvantage is the 'erase of natural colours' [13, 14, 33, 35, 36]]. Formaldehyde fixed organs display with a greyish monotone colour. Acetone or alcohol preserves the natural colours. They dehydrate the tissue and body cells, and induce poor cellular appearance under the microscope, and 'hard – to cut' organs. The used mixtures of fixatives are the first secret of whole body plastination [11].

Once the whole body is fixed, dissections to exploring and demonstrating the wanted effects will take place. This procedure might last for months dependent upon the wanted details and anatomic conditions.

The fixed, prepared and dissected body is then placed in a bath of acetone under freezing conditions. At low temperature acetone slowly replaces the cellular water. It will be later replaced by liquid polymers once the freezing atmosphere is heated up to the boiling point of acetone [11]. The liquid polymers are composed of silicone rubber, polyester and epoxy resins and injected through the vascular system.

The sequence of fixation, dissection, elimination of cellular water by acetone, and displacing the acetone by an appropriate mixture of resins includes the principal components of any

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'plastination'. Liquid resins might be hardened if exposed to 'hardening conditions' such as ultraviolet light, gas or heat. The whole specimen will become inflexible and remain in its wanted position or design 'for ever' [11, 15-17, 25, 26, 28, 30, 37].

Ethical considerations

Several religions consider the ‚opening of a corpse' such as autopsy a religious insult [17, 26, 28, 29, 31, 37, 38]. In general, religions distinguish between spiritual and fleshly issues, or – in other words - between functional (spiritual) and structural (fleshly, morphological) compartments [5, 11, 17, 29, 38]. The situation can be compared with the complex analysis of higher mathematics, which describes the conditions by real and imaginary numbers. It demonstrates that imaginary numbers might be mandatory to explain the solutions of certain complex functions, as originally explained by Leonard Euler in 1748 [39].

Most religions recognize that a living human does only live 'as a whole', and that a disturbance of the body will terminate its life (function).

Therefore, their deduction is logic that a dissection of the dead person might affect or even disturb the expected transfer of the 'dead' spirits into the eternal 'life'. Such beliefe includes specific ceremonies when passing away and has been reported from various ancient cultures, such as American Indians or Vikings [5, 6]. It is still present in several today's religions, priests, and believers [40-47].

Therefore, it is the 'duty' of any religion to convince persons who do not believe or believe in a different religion of the only right and successful method to 'reach the paradise'.

Therefore, the conflict between believers in a spiritual world and the deduction of potential benefits from corpses for still living persons is inevitable.

On the other hand the right of any man to gather as much information form himself and from its environment including his cohabitants founds the basis of natural sciences. It includes the predominance of mundane life when compared to spiritual worlds. As a consecutive, the integrity of a living person will end with its death at least if the community asks for information which can only be obtained from the corpse itself, for example to order an autopsy of criminal victims.

The observation that all structures in our environment possess an internal communicative space directs to a different aspect. The internal functions are related to their inner structures and might significantly differ from those of the environment [1, 2]. To investigate these functions requires analysis of their structures and consecutively autopsies or plastinates.

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How to use plastinates

Plastinates are preserved structures of dead persons. They do not demonstrate mental properties or even behaviour of the dead. However, they permit an insight into the complexity of our body, which is the prerequisite of any mental performance in our life. The expression of specific organ structures is not constant or independent from their functions. It depends upon their 'duties' to a certain degree. Examples such as perspiring during exercises or frighten eyes are well known.

These considerations might be expanded to ideas which sound strange at the first glance, such as the headline of the latest Body World exposure 'the anatomy of happiness' [48]. The rational argument is the observation 'that any happiness requires a healthy body' or at least an 'improvement of the acute health condition', for example the release of pain.

The theoretical 'immortality' and 'constant' visualization of functional appearance of plastinates is an advantage of plastinates when compared to conventional autopsies,

Well dissected plastinates allow an insight into the appearance of organs under these conditions and at 'times of rest' [7, 9, 11, 13, 17, 28, 30, 36, 49, 50]. Examples are shown in <figure 3, figure 4, figure 5>.

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Figure 3: Example of muscle tension at the start of running (picture taken at the Body World exhibition, Heidelberg, 2018).

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Figure 4: Example of Blood supply and 'coordinated thinking', (picture taken at the Body World exhibition, Heidelberg, 2018).

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Figure 5: Skeleton of a sitting body (picture taken at the Body World exhibition, Heidelberg, 2018).

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What is the message of these 'immortal' plastinates?

The first message includes the fact that the audience can explore the variety of organ structures, especially if an explanation of the derived functions is added.

A closer look takes the audience into inner organ structures which might express an unexpected heterogeneity. For example, the lungs might display with focally enlarged alveoli, occluded bronchi, or thickened walls of some arteries. The kidneys might include small cysts, or the brain focally atrophic gyri. All these alterations are of no impact on the health condition and do not affect the principle organ function, in contrast to tumour heterogeneity, which is suspicious to induce remarkable problems of tumor treatment [51] .

Both morphology and the daily observed person's reactivity tell the observers the natural laws of life. These include a hierarchical order of structures, the pathways of energy supply and communication, and the separation of an inner space form its environment by a communicative surface [1, 2].

The second message demonstrates the situation of the principle unstable equilibrium of life [1, 52, 53]. Nature has provided life with a broad buffer of organ structures in order to assure a reliable organ function. The liver can be reduced in size by about the half, one of the two kidneys can serve for organ donation, one, or at least the left lobe of the lungs can be excised, and all these organs will still perform the required body function without general restriction. The equilibrium ensures a stable function only inside its boundaries, or a short exceed within inertia [1, 11, 15-17, 25, 26, 28, 30, 37, 52, 53].

The functional boundaries guarantee a feedback only within the limitation boundaries. Once one of these boundaries and its inertia is passed the system leaves its equilibrium and bursts into a feed forward or 'self destructing' action [52, 53].

Examples are the occurrence of solid cancer, degeneration, infarction, or focal infections for example tuberculosis, which are demonstrated in <figure 6, figure 7, figure 8, figure 9, figure 10>.

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Figure 6: Plastinated brain section with enlarged gyri, natural colour.

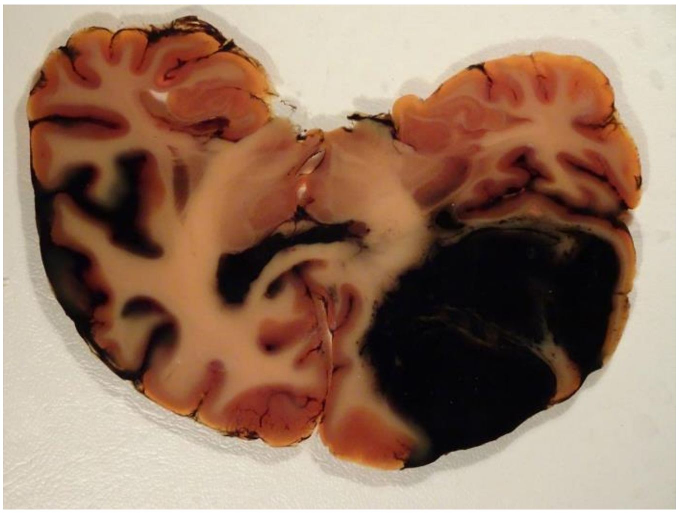

Figure 7: Plastinated brain section with subarachnoid hemmorrhage

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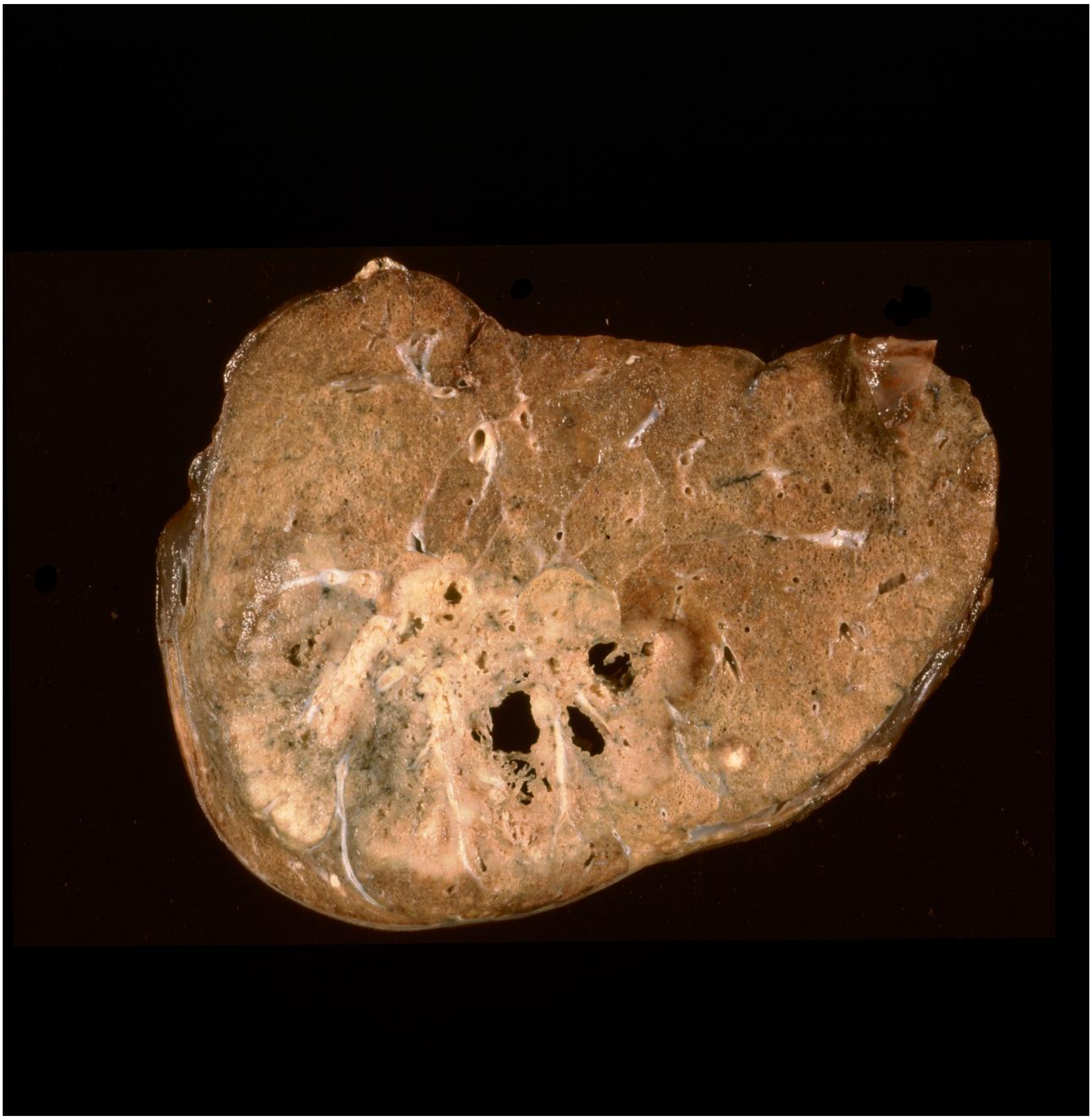

Figure 8: lung section showing a necrotizing bronchitis with actinomyces infection.

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Figure 9: Lung section showing a severe infarction and emphysematous altered lung tissue.

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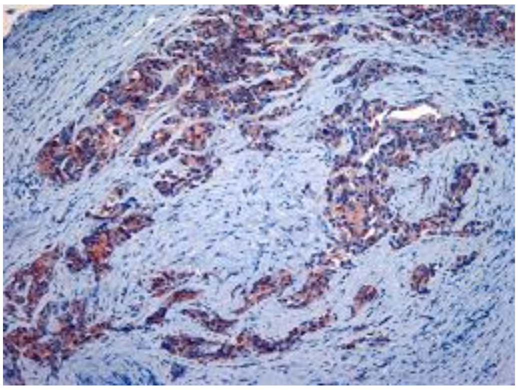

*Figure 10: Microscopic image of a metastatic adenocarcinoma of the lung into the pleura (DAB, CEA, *20). The carcinoma induces severe chronic inflammation.*

The third message is more sophisticated. It is related to hierarchic orders of structures and functions, and of their communicative pathways [52, 53].

It is equivalent to answer the question: Can, and, if yes, how can a small solid organ lesion induce a breakdown of life of the whole body, even if the existent reserves are obviously sufficient to maintain life? This question does not uncommonly arise in daily clinical practice. It is related to the question ‘what was the cause of death?’

The usual answer is ‘failure of the cardiovascular system’, which is a crude and obviously not detailed or explaining description. The detailed answer might be searched in the communicative pathways or signals between structures which are embedded at a different layer of orders.

Signals or communication ‘lines’ are also embedded in an unstable equilibrium, and, therefore, vulnerable to exceed their boundaries. Violation of their limits can create chaos within the connected items, and a complete collapse of the whole system. An explanatory example is the breakdown of a house of charts, if a certain chart is removed [52, 53].

Diagnosis and consecutive treatment of a patient’s disease follow this idea. They distinguish between individual ‘feelings’ (pain, consciousness) and objective data (results of external investigations). These start with gross ‘live investigations’ (CT, NMR, etc), and end in analysis of excised tissue specimens. These include tissue, cells, cellular and subcellular compartments (proteins, genes, DNA sequences, etc.), as exemplarily demonstrated in <figure 11 and figure 12>.

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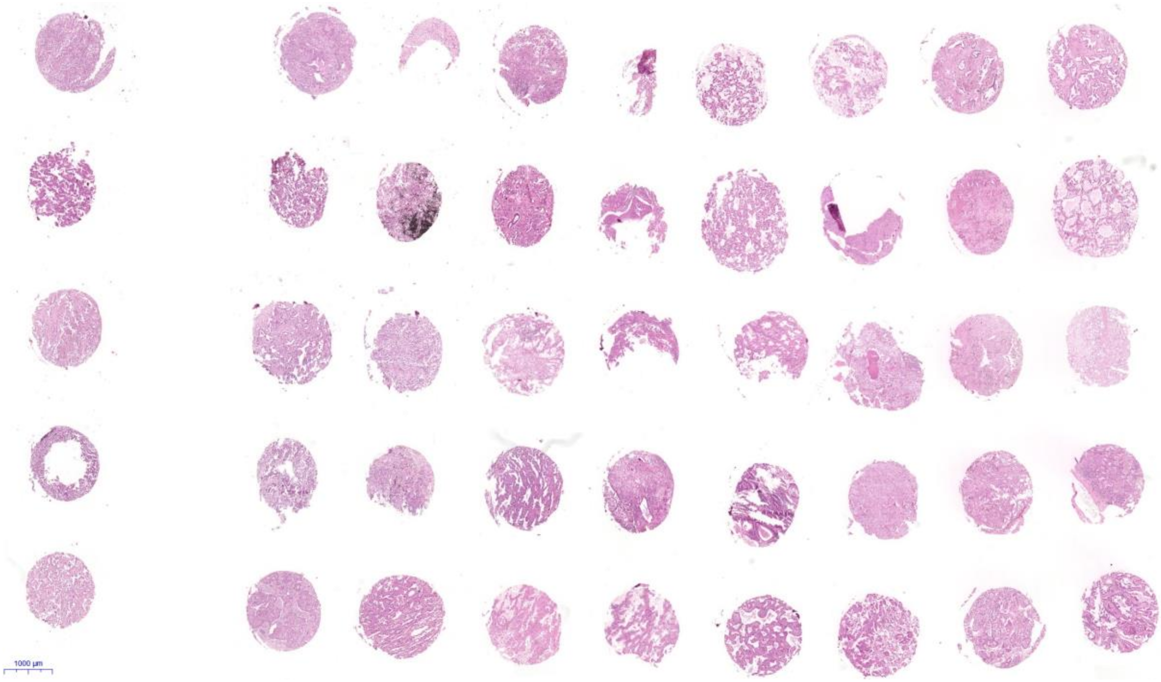

Figure 11: TMA sequence of a pulmonary adeno carcinoma sequence.

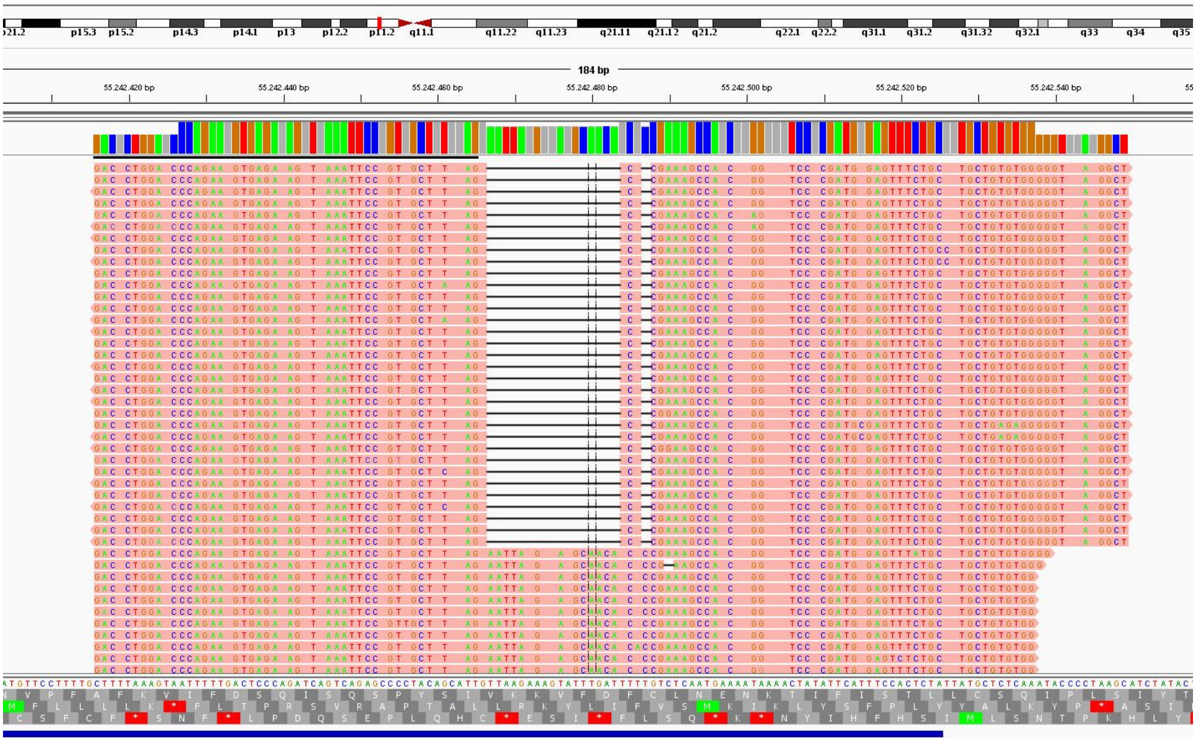

Figure 12: DNA sequence of of a deletion of Exon 19 in a pulmonary adeno carcinoma.

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These considerations indicate that plastinates are a useful and natural tool to demonstrate how our body is constructed, how it functions, and how it is embedded in the basic laws of our life, our society and natural condition.

Discussion

Our Western society demands a proper, future oriented education and instruction of its citizens under the principal condition that its democracy should not degenerate to a manipulation of sheep. One important task is the demonstration of natural laws and predefined rules of our environment which cannot be changed.

One of these rules is to acknowledge that life is embedded in a chain of communicative structures which provide and steer functions of an unstable equilibrium [[52, 53]]. Any of such a system will provide its correct service as long as the boundaries are not exceeded. A violation of the existing limitations will induce serious problems, and finally cause the collapse of the whole system.

Plastinates provide a proper example of our body structures that are responsible for our life. They contribute to education and instruction of young and grown up, non experienced and experienced, aware and unaware fellows in this way:

They are original and attractive in providing an insight into our body without destroying the communicative position of the organs. Careful and detailed preparation of the visualized organs allows the exemplary demonstration of the complexity and associated functions, as exemplary shown in <Figure 9>.

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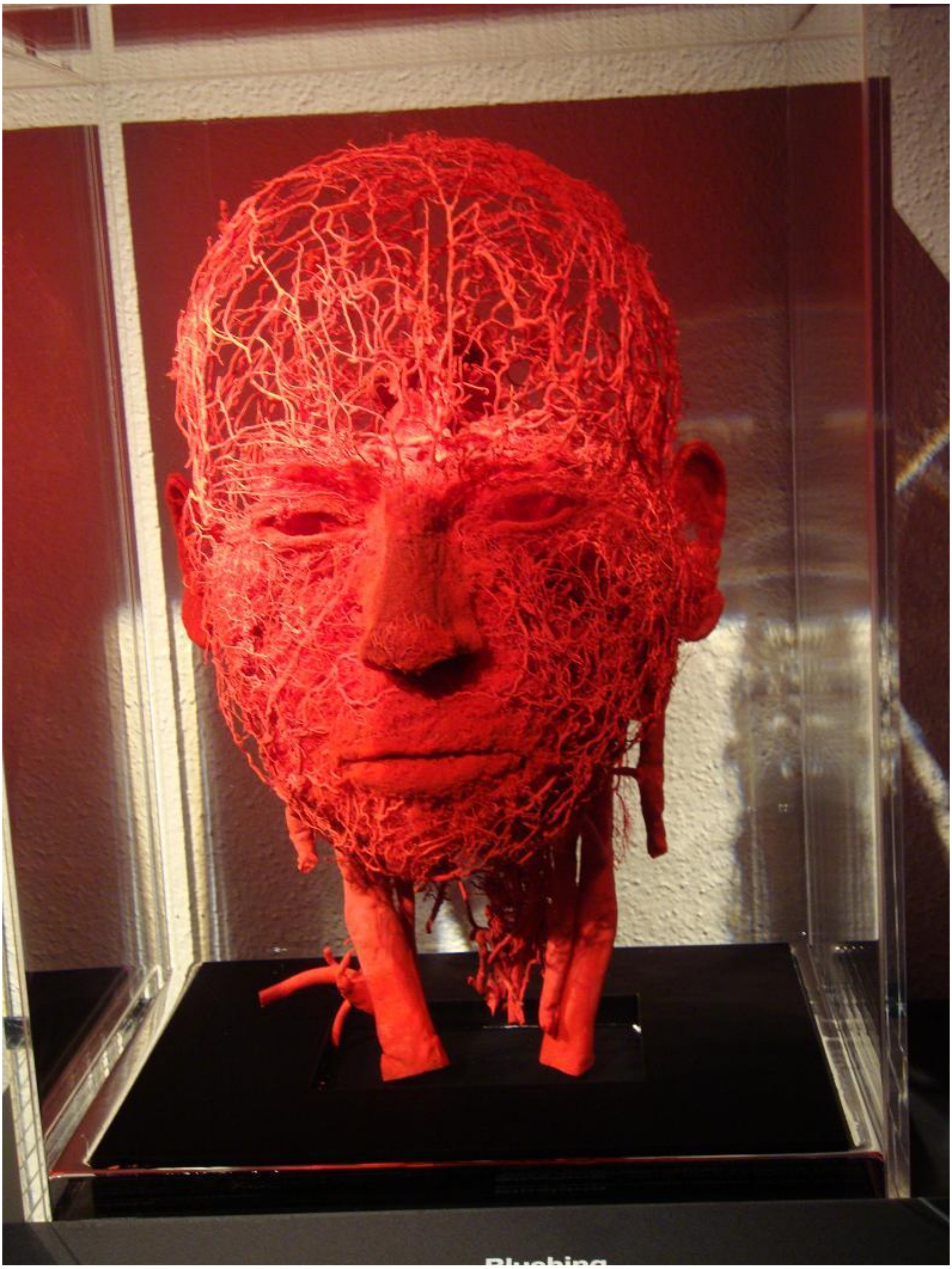

Figure 13: Plastinated head showing the dense network of blood vessels which assured the essential energy supply during its former life (picture taken at the Body World exhibition, Heidelberg, 2018).

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Detailed knowledge, experience in anatomy, as well as sophisticated and careful preparation of the bodies is mandatory to create these natural examples of our life. Autopsies serve for the explanation of an acute death, and cannot provide such an insight.

The exhibition of plastinates in combination with associated features such as organ failure, focal organ lesions, malformations, microscopic images, gene and protein analysis can successful amend the instructive effect of plastinates. In addition, they can serve for explanations of emotions, such as good luck, fear, or hate [[48]].

Solely visualization of knowledge without contemporary demonstration of the natural sources is exposed to misinterpretation, or even faked information. Therefore, electronic education and instruction cannot completely replace their mundane counterparts. These communication techniques are vulnerable to distribute fakes information or misinterpretation in principle [54].

Plastinates demonstrate the 'wonder of life' in a unique manner. Our body stays alive because nature has originated a complex system of structures, which consist of closed circumscribed compartments. They communicate and support each other. In anatomy, this idea of nature can be 'searched down' to the 'cell', the 'nucleus', the 'membrane', the 'chromosome', the 'gene', etc. It might be also extended to higher structures in human life, such as 'child', 'woman', 'man', 'profession', society', or 'language', 'intelligence', or even 'religion'.

All these items are alive at a vulnerable, unstable equilibrium and prone to dye if they exceed or disturb their natural boundaries. The whole body plastination possesses its natural boundaries too. It is limited by the ethics and behaviour of its environment, our understanding and explanation of nature, our forecast of future.

This technique can be a valuable instrument for tissue – based diagnosis, science research and dissemination. Plastination of organs or of the whole body is an additive method to the other techniques which are used for diagnosis in surgical pathology. Tissue – based diagnosis includes a forecast of the disease's development and an instruction for potential clinical or even social interactions. The more the patient knows and understands his disease the more appropriate are the consecutives of tissue – based diagnosis. The reasons are clear: Any diagnosis is based upon external investigations, and tries to reconstitute the equilibrium or normal functions inside our body.

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