CO_2 Balneotherapy for Arterial Occlusion Diseases*: Physiology and Clinical Practice

by

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Carbon dioxide, along with being the final product of metabolism and a basic ingredient of photosynthesis, is also a remedy which when applied to the skin has effects that are empirically held in high regard. Already in the Middle Ages, acidic water and gases vented from the ground (carbon dioxide fumaroles) were recognized to have strong curative powers and to be effective against "St. Anthony's fire" caused by ergot poisoning which often occurred at the time. There was no other effective method of treatment. In 1624, the medical scholar van Helmont (1577–1644) confirmed that these gases contained carbon dioxide. The anti-infective properties of carbon dioxide were discovered and analyzed by Boyle (1627–1691) and Lavoisier (1743–1794). The first systematic medical research of CO_2 use was conducted by Lalouette (1777), who showed that chronic and inveterate skin damage is cured by the serial application of CO_2.

Areas where CO_2-enriched water emerges naturally from the ground developed in the 19th century into curative spas for the heart. Because the method of using such water involved volumetric loading (pre-loading) in a full water bath, this at one point essentially appeared to fall out of date. However, the application of CO_2 to the skin gained a suitable degree of acceptance based on the experiences of physicians, and eventually came to be used as an effective mode of treatment for circulatory disorders, vascular disorders and disorders of autonomic function and regulation. The treatments took advantage of local features such as a spa cure or were carried out using "carbon dioxide springs" or (artificial) therapeutic CO_2 officially recognized as medications (Jordan, 1985).

Treatment involving the oral administration of CO_2-enriched water, that is, the drinking of carbonated water, is also sometimes carried out.

Formation of Carbon Dioxide

Highly concentrated CO_2 in the form of gas (carbon dioxide fumaroles) or dissolved in water forms as a magma product following volcanic eruption on the earth's crust. When these gas springs or source gases reach the earth's surface, the concentration decreases on account of the drop in pressure, or removal of the gaseous ingredients takes place according to the Henry-Dalton laws. This can be technically prevented. It is possible, at substantial cost, to artificially obtain a "supersaturated" CO_2 concentration beneficial for treatment.

CO_2 dissolution in water is primarily physical, with only 1 part per thousand chemically bonded to water as carbonic acid.

Aside from this, dissolution is influenced by the temperature and the substances dissolved in water, in accordance with the Gay-Lussac law. The carbon dioxide concentration decreases at reduced pressure, increased temperature, and in the presence of minerals.

Eighty percent of German natural mineral spas contain the minimum concentration of 400 mg CO_2 required for treatment (Hentschel, 1967; Schnizer, 1985). Of these, exactly two-thirds have a CO_2 level greater than the lower limit value of 1 g (per kg of water) required for designation as carbon dioxide-enriched water (German spa calender).

Table 1. Terminology

Carbon dioxide (Kohlendioxid):	Carbon dioxide used for medical purposes
Carbonic acid (Kohlensaure):	Historical expression. Only 0.1% in water is chemically bound as H_2CO_3 because 99.9% is dissolved as a gas.
Natural spring (sprudel):	Vernacular expression. Largely combined with acid.
Carbon dioxide spring (Sauerling, Sauerborn, Sauebrunnen, Sauerwasser):	Historically used according to personal preference in balneotherapy.
Carbon dioxide fumarole (Mofette):	Natural emission of gases
Dry gas (Trockengas):	A gas used for therapeutic purposes

Medical gases, such as Linde and Messer Griesheim, are pharmaceuticals listed in the German and European pharmacopeias (respectively DAB and Ph. Eur.). This artificially produced "dry" CO_2 gas, which is identical to the CO_2 released from naturally occurring gases vented from the ground and from carbon dioxide springs, is placed in special plastic bags (e.g., in Germany, Ehrlich Bad Wurzach; in France, Sinthylene Pont de Vaux) and used, the CO_2 and water being mixed with the use of an impregnation apparatus (e.g., Subaqua Emmendingen, Unbeshieiden Baden-Baden, Technica Ratzeburg).

CO_2-enriched water can also be produced by reacting a (bi)carbonate with a chemically equivalent amount of acid (aluminum sulfate, ammonium chloride, fumarate, sodium bisulfate, succinate).

This "carbon dioxide spring" is employed in the pharmaceuticals list as a pharmaceutical.

Respiration

Through oxidative metabolism, the human body produces 200–250 mL/min of CO_2 while at rest, and up to 1.5 liters/min under kinetic loading. CO_2 molecules, which are a ubiquitous constituent of the body, are water soluble and fat soluble, and pass freely through membranes at a rate 25 times higher than O_2. The movement of CO_2 in peripheral tissue and the lungs is determined by the pressure gradient between the tissue or alveoli and the capillaries. Under physiological conditions, 3% of the CO_2 passes through the skin and is released into the atmosphere (which generally contains 0.03 vol % of CO_2). The amount that is absorbed through the skin when the CO_2 concentration in the phase surrounding the body (gases or CO_2-enriched water) has been raised to a saturated state is at most 30 mL of CO_2 per square meter of body surface area per minute.

When arterial blood has the same CO_2 partial pressure as the alveoli of 40 mmHg, it contains 500 mL of CO_2 per liter. The amount of CO_2 present in venous blood at a partial pressure of 45 to 47 mmHg is about 50 mL higher (Jordan, 1985). From 5 to 10% of the CO_2 molecules in the blood are physically dissolved. About 10% form carbamino bonds with NH_2 groups, primarily in red blood cells. The remainder become carbonic acid (H_2CO_3) under the action of a carbonate dehydratase catalyst within the blood, following which the carbonic acid immediately dissociates into bicarbonate ions and hydrogen ions. HCO_3^- migration is the same as for chloride ions (Hamburg effect—chloride ion migration) (see Bauer et al., 1980).

According to {Harden?}, reduced hemoglobin binds with a greater amount of CO_2 than oxygenated hemoglobin. This facilitates CO_2 transport in the veins and the exhalation of CO_2 outside of the body. A rise in CO_2 directly lowers the pH and shifts the oxygen dissociation curve toward the right (Bohr effect). As a result, the oxygen binding power of the hemoglobin decreases, making the use of oxygen within the tissue easier.

CO_2 application to the skin raises the oxygen partial pressure not only of the skin but of the muscles as well (Komoto et al., 1986). CO_2 inhalation has the same effects on healthy individuals and on arterial occlusion patients (Fig. 3; Boekstegers et al., 1990).

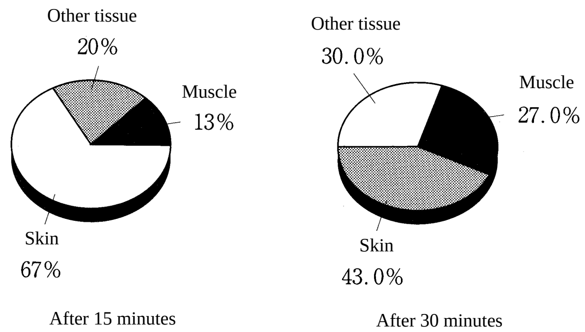

Fig. 1. CO_2 distribution 15 minutes and 30 minutes after completing CO_2 application.

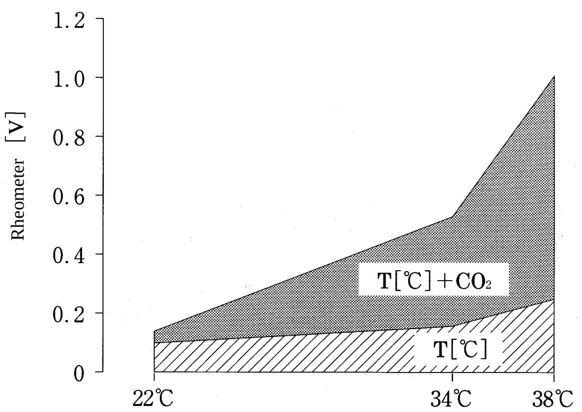

Fig. 2. Rise in dermal blood flow measured with a laser Doppler rheometer. Temperature change (T[°C]) versus temperature change + CO_2 (T[°C] + CO_2).

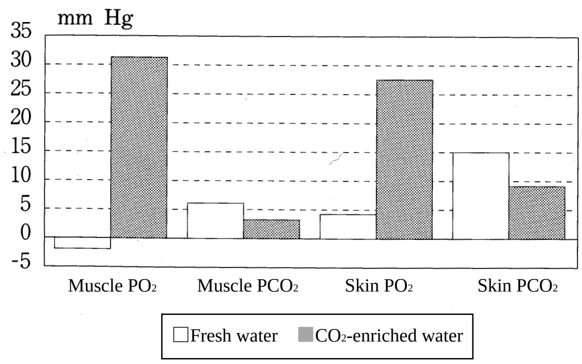

Fig. 3. Changes in O_2 partial pressure (PO_2) and CO_2 partial pressure (PCO_2) in muscle and skin directly measured with a mass spectrometer. Measurements were taken on rabbits at the end of a 30-minute fresh-water full bath and CO_2-enriched water full bath. (adapted from Komoto, 1986)

Hence, unlike in full, fresh-water bath, the O_2 partial pressure in the arterioles rises in an intermediate temperature carbon dioxide-enriched full bath. This is apparently based on stimulation of the respiratory centers or improved uniformity in the ventilation and perfusion of the alveoli (Jordan, 1985).

Hemodynamics

The rise in the CO_2 concentration within body fluids acts both centrally and peripherally. Chemical receptors are stimulated and sympathetic nerve activity rises, resulting in an increase in the vascular resistance of arterioles and veins other than the cutaneous veins (e.g., Cunningham 1987). The rise in CO_2 concentration within the tissue and peripheral blood vessels causes precapillary arterioles to dilate, thereby opening capillaries that were functionally closed. The same is true also when CO_2 is applied to the skin (Ito et al., 1989). The peripheral resistance decreases and the blood pressure decreases.

In CO_2 inhalation, first vasoconstriction occurs. Hence, this can be likened only in part to the effects of CO_2 application to the skin. Only once the tissue concentration of CO_2 has risen does vasodilation occur. This dilation is triggered even without a change in pH (e.g., Blair et al., 1960). Hypercapnia lowers the resistance of arteries in the skin and muscles. The arteries of the skin in particular dilate on account of the decline in pH that arises at the same time. This takes place even with CO_2 administration to the skin (Diji and Greenfield, 1960).

In a low-pressure system, local elevation in pCO_2 promotes a venous vasomotor response, regardless of the pH. Topical action and direct central action by hypercapnia causes the veins to constrict. Acidemia has a dilatative effect on the veins.

Blood Rheology

CO_2 has an influence on blood flow and blood coagulation. Whether CO_2 is inhaled or is applied to the skin, it promotes coagulation and normalizes the fibrinolysis inhibition state (Hartmann, 1993). Declines in the viscosity of blood and serum and the decline in hematocrit resulting from the serial administration of full baths or three-quarter baths brought about improvements in blood flow properties over a long period of time. The likely cause is that capillaries which had not been perfused were re-perfused with fluid low in cells and protein. This agrees with the pharmacological blood diluting effect (Ernst et al., 1990).

Intermediate Temperature, Metabolism, and Anti-Inflammatory Effects

CO_2 stimulates the warmth receptors in the skin and inhibits the cold receptors. As a result, carbon dioxide-enriched water feels about 2°C warmer than fresh water (Jordan, 1985).

In addition, CO_2 has an anti-inflammatory effect.

Changes in CO_2 concentration affect the intermediate metabolism. A rise in the CO_2 concentration brings about a rise in the serum phosphorus and in the lactic dehydrogenase. This is based on the inhibition of glycolysis or the promotion of glycogen formation (Plötner et al., 1990).

Mechanism of Action

In spite of the numerous clinical studies in the literature, the detailed mechanism of action is still a matter of speculation. The question that has been constantly debated up until now is whether CO_2 acts directly or through a mediator.

What is particularly apparent is that transcutaneously absorbed CO_2 has been demonstrated within the body beyond the period of exposure (Andrejew, 1990; Jordan, 1985).

Application

CO_2 is applied to the skin either as a solution in water or in a gaseous state. It is also sometimes additionally administered by inhalation. (Administration by inhalation is used either for diagnostic purposes or experimentally.)

The following factors influence the effects of CO_2 administration.

Table 2. CO2 Effects

- Anti-inflammatory effects
- Stimulation of warmth receptors in skin, inhibition of cold receptors
- Vasodilation (precapillary arterioles)
- Reconstruction of functionally closed capillaries
- Rightward shift in O2 dissociation curve
- Rise in venous response (“vein tension”)
- Improvement in blood flow properties
- Stimulation of sympathetic nerve system

Table 3. Dosage parameters and method of administration.

- CO2 concentration
- Media: water, wettened gas
- Temperature
- Surface area: partial bath or full bath
- Time: length of exposure, number of exposures, and interval between exposures

- CO_2 concentration
- Temperature
- Surface area
- Time (length of exposure, number of exposures, and interval between exposures)

The effects of CO_2 application are clearly influenced by the concentration. The threshold at which effects appear is 400 mg/kg water, with the effects increasing linearly up to 1,400 mg CO_2/kg water, after which they level off. The water temperature has an influence on these effects (Fig. 2). In healthy individuals, the strength of the effects reaches a plateau after 3 minutes. In patients with disorders of the arterial, venous or microvascular circulation, the time required to reach a plateau increases (Hentschel, 1967; Schnizer et al., 1985).

Effects have been demonstrated for natural CO_2-enriched water, CO_2-enriched water produced by the artificial permeation of gas, and chemically produced KAO-Bub® or Actibath®. These effects have not yet been demonstrated from other "CO_2 baths," and so what had been thought of as effects in these latter cases are unfortunately nothing more than assumptions or inferences.

The temperature of administration has been strictly set based on physics and thermophysiology. The temperatures at which natural or artificially produced CO_2 water and CO_2 gas are administered differ. "Dry gas" is used at 28°C when the degree of moisture is raised using water vapor. In places commercially operated as "gas bath chambers," this standard is often not observed (Krüger, 1979).

"Closed CO_2 gas therapy" originally arose in Marienbad and Royat Auvergne. It uses heat production and evaporation humidity or perspiration as the means for absorbing CO_2 through the skin (Bee et al., 1994). In addition, when CO_2-enriched water is employed, use is also made of fluid dynamics (hydraulic pressure and Archimedean buoyancy) and water temperature. The objective intermediate temperature (34.5°C) and the subjective insensible temperature clearly differ from those in the case of gas. In the use of CO_2-enriched water, it is possible to endure a colder temperature due to the shift in the insensible temperature. Moreover, because skin microcirculation is maintained, CO_2-enriched water is suitable for cooling. The indications and effects of CO_2 introduction (inhalation) are under debate. Up until now, there have been few experiments of the type conducted by the Lecomte (Liège) research team on experimental animals using nitrogen as the control (Konsensus-Konferenz, 1990).

The effects from topical application and full baths differ. The arterial blood pressure and rheology are affected only by the full bath. The local circulation dynamics are influenced by CO_2 application at that site. CO_2 baths are traditionally carried out for a short time, the consensus being to set the minimum period of administration at 20 minutes.

When CO_2 baths are used serially as in a cure, a minimum period of 10 minutes is required.

In addition to the specific action, the regulatory responses (accommodation, adaptation, habituation) to external stimuli must be considered from the standpoint of regulation training (Hildebrandt 1982).

Table 4. Indications and contraindications.

Reliable Indications:
- Arteriolar occlusion diseases
- Cutaneous microcirculation disorders
- Arteriolar hypertension
- Venous insufficiency (particularly cold water use; "vein protection" in heat transport)
- Mild to moderate heart failure (up to NYHA stage II)
- Painful dystrophy (Sudeck's disease), Stage I
- Fibromuscular pain
- Disorders in autonomic function and regulation
- When muscle training is inadequate or impossible

Questionable Indications:
- Cerebrovascular disorders

Contraindications:
- Hypercapnia (cases where water baths are contraindicated)

Contraindications under Debate:
- Arteriolar hypotension

Indications and Contraindications

Table 4 presents a list of indications and contraindications compiled at a research meeting.

CO_2 therapy improves microcirculation in the skin and

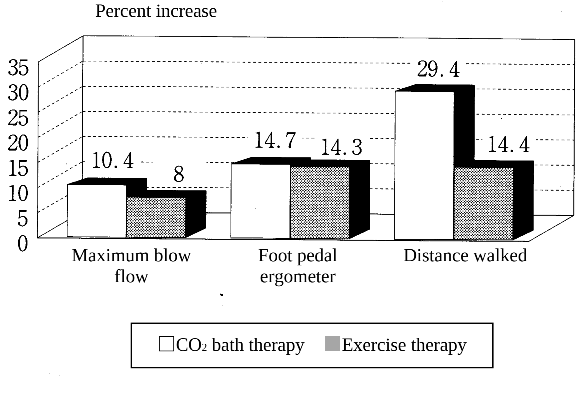

Fig. 4. Comparison of exercise therapy and CO_2 bath therapy. Changes in maximum arteriolar blood flow (mL/100 mL•min) after obstruction of blood flow, foot pedal ergometer (w), and walking distance (m) are shown in percent. (adapted from Beutel and Sobanski, 1985)

blood flow in the limbs and the entire body of patients with arterial, venous and microcirculation disorders. The strongest effects occur during the bath, but there are also effects after the bath. Moreover, with serial use, there are long-term effects.

Arterial Occlusion Diseases

Arteriolar blood flow is improved in both a CO_2 gas bath and a carbon dioxide water bath (Beutel and Sobanski, 1985 and 1980). Fig. 4 compares the effects of CO_2 baths and exercise therapy in a patient with Stage II intermittent claudication by examining the values used to assess treatment; namely, reactive congestion following blood flow obstruction, ability to walk, and ability to move the calf muscles as measured by foot ergometry. These values clearly improved more from serial CO_2 application than from exercise therapy. Further study is probably needed (e.g., Fabry et al., 1985; Krüger, 1979).

The vasodilation observed in application to the body's surface is limited to the areas of application. Local increases in blood flow occur without a drop in the blood pressure and without a "stealing" effect or a "borrowing-lending" effect (May, 1980).

CO_2 partial baths according to Cobet and Ratshow are classical uses for Stage IV necrosis. The effectiveness of applying CO_2-enriched water has also been demonstrated by carefully conducted clinical research (e.g., Wernerl et al., 1990). The mechanism of action involved in the application of CO_2 to the skin has not yet been elucidated, but a clear effect exists also in diabetic microvascular disorders. Here, the rightward shift in the O_2 dissociation curve and a mechanism similar to that discussed by Mucha (1992) concerning the therapeutic effects in painful dystrophy is problematic. Vasodilation at the ends of the limbs is suitable for the treatment of functional and morphological blood flow disorders at the ends of the limbs (primary, secondary Raynaud's syndrome) (Diji and Greenfield, 1960; Hartmann et al., 1995). Topically applied CO_2 improves blood flow in the hands and fingers and also improves subjective symptoms, in addition to which it lowers the severity of the symptoms and reduces the frequency of attacks.

It is not yet known to what degree the application of CO_2 to the skin affects cerebral blood flow. This is most likely governed by the method of administration (e.g., Jordan, 1985). In Eastern Europe, CO_2 full baths are believed to be indicated for cerebrovascular disorders and disorders in brain function. (Florian et al., 1990).

Arteriolar Hypertension

The decrease in the peripheral vascular resistance from a CO_2 bath is the reason for its use in the treatment of arteriolar hypertension. However, in borderline hypertension patients, because the cure is accompanied by weight reduction and salt restrictions, it has been impossible to ascertain the effects specific to CO_2 (e.g., Hartmann et al., 1989).

By contrast, in patients with clear hypertension, following several weeks of regular CO_2 application, the blood pressure at rest decreases. At the same time, peripheral microcirculation improves and peripheral vascular resistance decreases (Winterfeld et al., 1990). This fact is supported by numerous research on classical indications and long experience with combined treatment based on a "carbon dioxide spa."

Heart Disease

Full baths in fresh water and full baths in carbon dioxide water are contraindicated for severe heart failure, coronary disease and arrhythmia. The period of initial onset during which peripheral resistance has not yet decreased is particularly dangerous. However, a partial bath with CO_2 or a gas bath are being used for patients with mild heart disease. Patients with NYHA stage II or III heart failure following myocardial infarction undergo a 6% rise in peripheral O_2 use with CO_2 administration (Knopf et al., 1989).

In cardiac hypoxia, the CO_2 application increases stroke volume and cardiac output, and at the same time decreases heart rate and peripheral resistance. In parallel with this, patient mobility as measured with an ergometer improves. These changes are accompanied at the same time by alleviation of the angina pectoris symptoms (Sorokina et al., 1985; Sorokina et al., 1985).

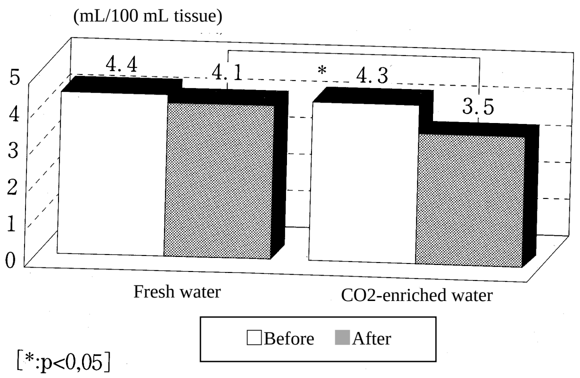

Fig. 5. Decline in venous volume increase measured by venous occlusion plethysmography. Comparison of the effects of continuous fresh water bath and CO_2-enriched bath (34.5°C, 12 baths over 3 weeks).

Venous Circulation Disorders

CO_2 has a vein protecting effect in heat transport (Hartmann et al., 1993). The improvement in venous function resulting from CO_2 application to the skin has long been debated on theoretical grounds, but no conclusion has been reached. Clinicians support the existence of this effect, but basic medical researchers deny any such effect. According to reports by a French research group, repeated baths in 35 to 37°C carbon dioxide-enriched warm mineral water brought about improvements in varicose veins and venous function in post-thrombotic syndrome (Garreau and Garreau-Gomez, 1985; Peanne, 1989). Functional improvements following CO_2 application in a cure correspond to the results of repeated cold stimulation by the pouring of 15°C water. Heat is removed countercurrently at this time (e.g., Hartmann, 1993).

Cold and hydrostatic pressure are used in lower leg baths within 28°C carbon dioxide-enriched water for varicose vein and post-thrombotic syndrome patients. It is not clear whether the CO_2 has an additional effect. There does exist a clear difference in the water temperature that is subjectively agreeable. Fresh water at 28°C is not agreeable. Fig. 5 compares the effect of serial CO_2 full baths on venous volume with the effects of fresh water full baths at the intermediate temperature of 34.5°C. A specific CO_2 effect can be clearly demonstrated from this. The vein protecting effects of CO_2 in external heat transport following 20 minutes in a mineral-warm-exercise bath containing 600 mg CO_2/kg water adjusted to 36°C could probably be demonstrated by a before and after bath comparison. However, because heat transport poses a risk to the patient, ethical considerations made it impossible to conduct controlled trials (Hartmann et al., 1993).

Painful Dystrophy (Sudeck's Disease)

In Stage I painful dystrophy, the application of CO_2 to the skin alleviates pain, clinical improvement in function is observed and recovery clearly speeds up, lowering treatment costs. Reasons that are currently under investigation are a relaxation in autonomic nervous system tension, absorption of edema accompanied by normalization of substance exchange, and the elimination of painful sensations due to the decomposition of pain-causing substances.

Fibromuscular Pain

While effects upon painful dystrophy have been demonstrated through methodical research, therapeutic effects have not been demonstrated in "soft tissue rheumatism," which is familiar from long experience.

The effects against anomalies in autonomic nervous system regulation ("autonomic function imbalance") are the same, and so it is hoped that an effective method of treatment which incorporates the positive effects of fresh water baths will be developed.

Conclusion

CO_2 is a natural, chemical and technical therapeutic means which is effective and has no side effects when used for the proper indications and in the proper dose. At the same time, in spite of the many studies that have been conducted on CO_2 therapy, a general consensus has yet to be reached on optimal dosage and detailed differential diagnosis. Studies are currently underway by an international research group to demonstrate the effectiveness of CO_2 therapy and to establish standards and criteria, a concern that has long been neglected.

Together with clinical studies such as this, research is also being conducted on the mechanism of action using precise techniques in which advances have recently been made. Sufficient scientific clues exist for this purpose. CO_2 bath therapy can be regarded in the same light as therapies based on bodily activity (sports therapy, work therapy, training therapy, movement therapy) because it elicits the same physiological responses, such as active changes in cutaneous blood flow and muscle blood flow.

CO_2 bath therapy can be practically applied in a variety of ways. It is a particularly important therapeutic approach for patients incapable of sufficient muscle activity on account of aging or diseases of the support and locomotor systems, and is especially helpful for functional recovery in physical medicine and rehabilitative medicine. In this sense as well, there is much significance in shedding light on the essential nature of current research topics and in seeing these to a successful completion.

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