Cervical disc herniation is due to cervical disc protrusion oppressing adjacent cervical nerve root and degeneration of nucleus pulposus by rupture of the fibrous ring releasing inflammatory mediators stimulating cervical nerve root or sinuvertebral nerve, which cause neck and shoulder pain, radicular pain and numbness of upper extremity, or accompanied by a series of symptoms such as dizziness, headache etc. It has been clinically proven that target radiofrequency in the treatment of cervical disc herniation is effective[1-3]. A large number of references support the ozone play a positive roll in the treatment of cervical disc herniation[4-6].

There were 150 CDH cases treated by targeted radiofrequency combined with epidural ozone injection from October 2011 to October 2014 in our hospital. Now the observation of curative effect and the distribution and excretion of the injected ozone are reported as follows:

1. Clinical data
   1.1 General data
   Our data includes 78 male cases and 72 female cases with the age of 38~68 years and disease duration of 3 months~5 years. Of which (1) cervical spondylotic radiculopathy: 66 cases. Neck and shoulder pain radiate to the shoulder and upper extremity accompanied by hand numbness, limitation of neck movement, nerve root traction test (+), Spurling test (+). (2) cervical spondylotic myelopathy: 6cases. Neck and shoulder pain accompany with numbness of limbs, rigidity or weakness, sensory disturbance in individual patient. (3) arteria vertebralis type: 28 cases. Patients with headache, nausea, numbness of limbs, attack with turning head. (4) sympathetic type: 15 cases. (5) cervical type: 10 cases. (6) mixed type: 25 cases. Symptoms often combined with the above two or three types. All cases have been treated conservatively with taking analgesic, traction, physical therapy etc before the treatment, the treatment results were poor. All patients were diagnosed with cervical disc herniation by X-ray on frontal, lateral and double oblique position and CT and MRI of cervical spine. And the following were regarded as operative contraindicated objects: (1) who with severe cervical spinal stenosis and calcification of the posterior longitudinal ligament; (2) with severe cervical disc protrusion; (3) with severe hypertension; (4) with uncontrolled diabetes; (5) with coagulation dysfunction; (6) with systemic infection or infection at the intended site of the puncture.

   1.2 instruments and equipment
   medical purified oxygen. Ozone generator (Germany Herman). Radio frequency therapy device (Baylis).
somatom emotion CT (Siemens).

1. 3 method
(1) patient or authorizer signed the preoperative informed consent; (2) based on preoperative X-ray on frontal, lateral and double oblique position and position of MRI of cervical spine localizing protruded intervertebral space; (3) patient lay on the CT table, shoulders padded high, neck lean slightly back and the head was fixed on the CT head-rest with wide tape; (4) first, confirm the pathological intervertebral space by CT scout image, then conventional scanning of protrusion of intervertebral space with the slice thickness of 2mm, select the corresponding layers used for targeted radiofrequency puncture from the resulting scanning sequence, and design the puncture path on the selected puncture layer: take the protrusion as puncture target to determine the best skin needling point and measure the depth and angle of the needle ( see Figure 1 ); (5) after routine disinfection and sterile draping, perform local infiltration anesthesia on the selected spot, push aside the trachea and carotid artery, insert the needle according to the designed puncture path, scan and observe again when the needle insert into the disc, then adjust the direction and depth of the needle until it reaches the target (see Figure 2); (6) after confirm the tip of needle succeeded in reaching the target by CT, perform routine high and low frequency electrical stimulation test, reconfirm the tip of needle is not near the spinal nerve ( 50Hz, 2mA test, without tingling of the corresponding spinal nerve distribution area; 2Hz, 3mA, without beating of muscle innervated by the corresponding spinal nerve ), then perform frequency ablation at 90°C last 300s. Observe the patient response closely during the treatment. If patient without discomfort or only have warm sensation on the neck and shoulder, then continue the treatment with radiofrequency ablation. Terminate radiofrequency ablation immediately once patient complained of burning sensation and numbness of upper and lower extremity. Adjust the position of needle’s tip, perform the electrical stimulation test again until the completion of radiofrequency ablation. Try to inject normal saline through the radiofrequency needle after the treatment. Push the tip of the needle forward 1–2 mm if can’t. When blood and gas are not drawn out after breaking through the protrusion or fibrinous ring, inject normal saline 2ml (containing contrast medium iohexol 0.2ml ), perform CT scan again, observe that the contrast medium has a banding distribution in the anterior space of dural sac (see Fig. 3), inject ozone (50ug/ml) 5ml and withdraw the needle. Attach the bandage to the puncture point on skin, perform CT scan again and observe the distribution of the injected ozone ( see figures 4 and 5). The patients’ BP, HR, SpO2 were continuously monitored during the treatment. Lay in bed for 24h after the procedure. And perform cervical CT scan and 3D reconstruction 24h, 72h after the treatment. Wear cervical supporter for 1m after discharge. Evaluated the curative effect of the patients in the follow-up.

2. Results
The group of 150 patients all underwent puncture successfully till the target and completed the radiofrequency ablation treatment under CT guide without injuries of carotid artery, spinal cord, nerve root and infections of intervertebral space. The injections of normal saline 2ml containing contrast medium were all distributed in the anterior space of dural sac, no case was found punctured into subarachnoid space. The 3D reconstruction immediately after the injection of 5ml ozone showed the longitudinal distribution of low density gas shadow along the anterior space of dural sac, up to C2 vertebral body and down to T4 vertebral body (see Figure 6), small residual was found 24h later after operation by 3D reconstruction (see Figure 7), and the low density gas shadow almost disappeared 72h later after operation (see Figure 8). All patients were followed up for 6 months, according to clinical diagnosis, adapting Odom’s evaluation standard to evaluate, 52 cases were excellent, 68 were good, 16 were fair, 14 were poor, the rate of excellent and good was 80%. There was no case of contrast medium or ozone injected wrongly into the subarachnoid space.

Figure 1: selected the penetrating layer and designed the puncture path ( took the disc tissue which broke into the spinal canal as puncture target, designed puncture path, 1 represented depth of needle, 3 represented angle of needle )
Figure 2: inserted the needle to the target according to the designed puncture path under CT guide.

Figure 3: confirmed the tip of needle locate in the anterior epidural space (the contrast medium had a banding distribution in the anterior space of dural sac)

Figure 4: injected ozone into intraspinal canal (shadow on both sides of the protrusion represented the injected ozone)

Figure 5: the distribution of ozone in the spinal canal (the injected ozone distributed in the anterior epidural space)
3 Discussion
Cervical disc herniation is a common vertebral pain source. In addition to a small part of sever protrusion causing compression of cervical spinal cord or cervical spinal nerve root which require surgical treatment, the vast majority of mild, moderate protrusion may relieve symptoms by targeted radiofrequency thermocoagulation treatment\[^{1-3}\]. But the range of radiofrequency thermocoagulation is relatively limited, inactivation of inflammatory factors which have spread is often not thorough. Ozone is a strong oxidant composed of three oxygen atoms and has a strong oxidative ability, which is after fluoride and persulfate in the third place. Injections of ozone into the disc have a direct effect on proteoglycan of the nucleus pulposus of intervertebral disc, lead dehydration and subsequent degradation of cell matrix, damage proteoglycan of the nucleus pulposus and nucleus pulposus cell, reduce the capacity of the disc, thus reduce the compression of the nerve root. The contraction of the intervertebral disc decreases the venous congestion caused by compression, improves local microcirculation, increases the oxygen supply. Medical ozone also has analgesic and anti-inflammatory effects, inactivates inflammatory factors releasing from the protruded disc, thereby eliminates the inflammatory pain of intervertebral disc herniation. Ozone can also inhibit the synthesis of prostaglandin, inhibit the release of bradykinin and pain complexes, and increase the release of antagonist or soluble receptor neutralizing hormones of pro-inflammatory cell such as interleukins\[^{4}\], thus release the pain. Through controlled clinical trials, Cheng yahua etc. found that epidural injection of ozone and diprospan can effectively relieve the pain of patients with cervical spondylosis\[^{5}\]. Su Qichao et al found that it was benificial to fully contact with each other of herniated nucleus pulposus and ozone by injection of ozone to the location of disc herniation through the anterior space of dural sac\[^{6}\], so as to achieved a more thorough treatment effect.

The group of patients underwent targeted radiofrequency ablation to the herniated cervical intervertebral disc, after that, 5ml 50ug/ml medical ozone was injected into the anterior epidural space of the herniation. Not only
can further melt herniated disc tissue, inactivate related inflammatory mediators, and also separate the dura membrane and nerve root of the corresponding segments and the protrusion completely, forming a isolated buffer cushion between them, play a similar role as polyester cotton piece in in二者之间形成一个隔离缓冲气垫, 起到类似于三叉神经微血管减压治疗三叉神经痛时所用的涤纶棉片的隔离缓冲作用[7,8], 从而达到比单纯射频或单纯注射臭氧更好的效果。

Ozone has a temperature dependent half-life, it's hard to store, and there is no report in literatur about how long the ozone which is injected into the anterior epidural space will remain, so we performed follow-up CT scan to observe the distribution and excretion of ozone in the anterior epidural space. By dynamic scan observation, we found that the ozone may distribute widely in the anterior space of dural sac, up to C2 vertebral body and down to T4 vertebral body with the injection 5ml ozone into C5/6 vertebral space, it separated the anterior margins of the dural sacs and nerve roots of corresponding segments and posterior longitudinal ligament completely. It effectively cushioned the nerve compression of the protrusion.

The excretion time of ozone is about 72hrs, it remind us that if we inject ozone into the anterior epidural space repeatedly, the injection interval is 72hrs at least.

When any treatment technique is used in clinic, its safety weight is more important than its efficacy as the main index of evaluating its quality. As a strong oxidant, medical ozone can effectively melt the herniated discs organism and eliminate local inflammatory mediators to achieve therapeutic effect. It will bring disastrous consequences of central nervous system if we inject ozone into subarachnoid space carelessly. Our therapy team have successively carried out a variety of minimally invasive treatment under CT guide [9-21]. We found that the puncture performance under CT guide can be accurate to mm level. Thus, for safety purpose, this treatment should be operated under CT guidance, and before the injection of medical ozone into the anterior epidural space, the normal saline containing contrast agents should be injected first, and confirm the liquid can't be injected into the subarachnoid space by CT scan, then inject low concentration ozone carefully.

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